MERCK'S BULLETIN

A Periodical Record of New Discoveries, Introductions, or Applications of Medicinal Chemicals.

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NOTICE TO SUBSCRIBERS.

The pressure of *New Matter* crowding upon the pages of this periodical has caused me to *change its mode of publication* from a "Bi-monthly" issue (appearing every *second* month), as hitherto, into a MONTHLY.—*From the present number*, the "BULLETIN" will be issued *every* month; *no change* taking place in the *Subscription Price*, which remains ONE DOLLAR PER YEAR, as before. E. M.

Entered at the Post-Office, New York, as Second-Class Mail-Matter.

Acid, Agaricic (Laricic)—$C_{14}\ H_{27}\ (O\ H)\begin{cases} C\ O\ O\ H \\ C\ O\ O\ H \end{cases}$—This substance forms *the active constituent of* AGARICIN, which is obtained from the officinal *Fungus Laricis* (White Agaric).

Pure AGARICIC (or: LARICIC) ACID melts at 138° C [280.4 F], and is but slightly soluble in *cold* Water; more easily so in *hot.* The hot aqueous solution is limpid, prone to form froth on agitation; and, on cooling, drops the major part of the Acid in a finely crystalline form.

The physiologic and the therapeutic action of AGARICIC ACID have recently anew been made the subject of exact investigation, by FRANZ HOFMEISTER (*Archiv für experimentale Pathologie und Pharmacologie*, 1888; Band 25, p. 189). His researches confirm the earlier ones of J. M. YOUNG (*Glasgow Medical Journal*, 1882; Vol. XVII, p. 176) and NORRIS WOLFENDEN (*Medical Times and Gazette*, 1881; Oct. 1st).

The principal results are these:—

1,—AGARICIC ACID is **an eligible Antidiaphoretic,**—*coming fully equal to* ATROPINE, in the effect of suppressing dermic secretion;—

2,—The usual **Vomitive and Diarrheal effects** of AGARICIN are **perceptible in but very faint measure** when *Chemically Pure* AGARICIC ACID is administered.

Prof. KAHLER reports *a decided Antidiaphoretic effect without any hurtful accessory action,*—consequent on dosages of 0.02 and 0.03 gramme [⅓ to ½ grain], with a daily maximum of 0.1 gramme [1½ grain], of AGARICIC ACID.

Hence, AGARICIC ACID appears to be eligible as a *safe and certain* remedial agent in the debilitating *Nocturnal Sweats of Phthisis.*

Allyl Tri-bromide—$C_3\ H_5\ Br_3$—has been obtained by WURTZ, by treating Allyl Iodide with Bromine. It is *identical with* the so-called **"Tri-brom-hydrin,"** which was previously obtained by BERTHELOT and LUCCA, by the action of Phosphorus Tri-bromide and Phosphorus Penta-bromide on Glycerin.

ALLYL TRI-BROMIDE is a slightly yellowish liquid, of specific gravity 2.430 at ordinary temperature, and boiling at 217° C [422.6 F].

The therapeutic properties of this substance were recently investigated by ARMAND DE FLEURY, who assigns to it a position of decided merit in Therapy *for its energetic* **Sedative** *and* **Anodyne** *action.* He

Coronillin — $C_{11} H_{12} O_5$ — is a GLUCOSIDE recently discovered by SCHLAGDENHAUFFEN and REEB in the European PAPILIONACEA : *Coronilla scorpioides.*

By boiling with dilute mineral acids, CORONILLIN splits up—as all Glucosides do—into a Derivative Substance and a Sugar. This *Derivative* of CORONILLIN has been named **Coronillein.**

The *physiological* properties of these two substances are widely different. The Glucoside—CORONILLIN—is a **Heart-poison,** of action similar to that of DIGITALIS; while its Derivative—CORONILLEIN,—by virtue of its constitutional stability, passes through the organism entirely undecomposed, and consequently exercises *no toxic action whatever.*

Di-phenyl-methyl-pyrazole has recently been lauded as a *Succedaneum for* ANTIPYRINE. It is distinguished from the latter by its very decided basic character, and by a less energetic reaction with Ferric Chloride. It appears in the form of white needles, melting at 150° C [302 F] ; difficultly soluble in Water, in Ligroin, and in Ether ; easily so in Alcohol and in Glacial Acetic Acid.

Eserine-Pilocarpine in Horse-Colic.—(*Additional to* **"Physostigmine,"** *in* BULLETIN *of Oct., 1888:*)—Researches by ELLENBERGER (*Archiv für wissenschaftliche und praktische Thierheilkunde*, 1887; Band XIII) and E. BASS (*Thiermedizinische Rundschau*, 1888; Band II, No. 18) have demonstrated the eminently beneficial action of **a mixture of Pilocarpine with Eserine** (PHYSOSTIGMINE) in the Colic of Horses.

In response to the numerous requests thereupon addressed to me, I have recently prepared such a mixture, *in proportions such as experience has shown to be possessed of the most desirable remedial properties for Veterinary Practice.* I have called this mixture "ESERINE-PILOCARPINE."

It is a white powder, very readily *soluble in Water.* The method of its *Injection* is the same as that for PURE ESERINE (and as indicated in the October BULLETIN of 1888).

The Dose of ESERINE-PILOCARPINE per injection is of 0.4 gramme [6 grains]; dissolved in 5 cubic centimetres [80 minims] of Water.

With young animals, however, 3 grains of the drug per injection may be sufficient.

In order to facilitate dispensation, ESERINE-PILOCARPINE is handled by the Drug Trade in ready put-up tubes of 0.4 gramme contents.

Hedwigia balsamifera is the name of a TEREBINTHINACEA, native in the West-India Islands.—In its *alcoholic extract*, GAUCHER COMBEMALE and MARESTANG have found *a Resin and an Alkaloid, both* of which exercise *toxic action*,—the Alkaloid more strongly so than the Resin.—The effects of both substances were found to be: Spasms, Paralysis, Reduction of temperature; finally: *Paresis of the heart*, Irregularity of respiration,—resulting in death.

The *Aqueous* extract of HEDWIGIA BALSAMIFERA is 2½ times less strong in its toxic action than the *Alcoholic*. The *stem* of the plant yields more toxic effect than the *root*.

Mercur-Thymol (*Thymol-Mercury*) **Salts:**

Mercury Thymol-Acetate;
" " -Sulphate;
" " -Nitrate.

These new preparations of mine having been subjected to preliminary experimental trials by Prof. Dr. KOBERT, of DORPAT UNIVERSITY, which demonstrated *their general eligibility* in the treatment of **Syphilis** beyond peradventure,—I thereafter requested Drs. JADASSOHN and ZEISING, of Prof. NEISSER'S CLINIQUE at Breslau, to institute a series of special investigations on the same subject. The results were fully reported in pages 781–819 of the *Vierteljahrsschrift für Dermatologie und Syphilis*,—whence the following statements have been condensed:—

In these clinical experiments, the three above-named MERCUR-THYMOL salts were investigated each singly, but all were exhibited in like manner. The ACETATE ($C_{10}H_{13}O\,Hg$—$Hg\,CH_3CO_2$) was, however, the one most largely worked-upon.—All three of the salts named are *crystalline*, *colorless;* insoluble in Water, but *easily soluble in Alkaline solutions.*

These MERCUR-THYMOL preparations were exhibited in two directions : *subcutaneously* and *internally.*

The **Subcutaneous** injections were usually made of 0.1 gramme [1½ grains] of MERCURY THYMOL-ACETATE suspended in 1 gramme [15 grains] of *Liquid Paraffin.* They were introduced between the muscular strata of the Gluteal region,—taking care to place the puncture as high up as possible ; which mode of proceeding involves the least amount of inconvenience to the patient, especially in ambulatory treatment.—These injections were repeated at intervals of 3–5 days; and complete cures were attained, in periods varying from 22 to 34 days,—thus requiring from 6 to 8 injections, and introducing about 0.34–0.46 gramme [about 5¼ to 7⅛ grains] of *Mercury metal* into the organism, in each case. (The proportion of *Mercury* contained in the *Thymol-Acetate* is 56.9%.)

The *unparalleled slightness of the local irritation* induced by these injections enables the physician, however, if opportunity for the stated number of applications be lacking, to *reduce the frequency of application,*—while increasing the dose proportionately, thus maintaining the given average of total dose for the period of treatment. For, as soon as one or two injections have been made, and are well borne, there is no danger in applying two, of 0.1 gramme apiece, in immediate succession, or giving one of, say, 0.15 gramme instead of 0.1, and then allowing a correspondingly longer pause before the next application.

There was *no appreciable difference* observed in the efficacy of the three salts above named.

The clinical observations made are resumed in the following theses:

> "1. Intramuscular injections of MERCUR-THYMOL salts are *more rarely and in less degree attended or followed by pain or by infiltrations*, than those of ANY OTHER of the hitherto usual insoluble Mercury compounds.
>
> "2. The various manifestations of **Syphilis** are thereby *rapidly and energetically subdued*, with no more than 6–8 injections for a cure."

(The *cleansing of the syringes* is best performed by passing *Liquid Paraffin* through them after each application, and keeping them immersed in the same liquid, in a covered vessel, until the next occasion for use.)

— The **Internal** medication by the MERCUR-THYMOL salts was tested *separately* from the injections. *Milder* cases of **Syphilis** yielded also to this exclusive treatment, although somewhat more slowly than to the subcutaneous method. *Tumescence of the gums did not survene* in any instance, even after several weeks' treatment. The salts were administered in pills, containing ½–1 centigramme [$\frac{1}{13}$–$\frac{1}{7}$ grain] each. In some cases this medication was continued for several weeks, at rates running up as high as 12 centigrammes [1⅞ grains] per day.

— — Messrs. JADASSOHN and ZEISING have, besides, made *Injection experiments on Animals* (rabbits) with these MERCUR-THYMOL salts, in order to gain information as to the RESORPTION OF INSOLUBLE MERCURY-COMPOUNDS in the organism.

Microscopic examinations of transverse muscle-sections taken from thus injected regions at various periods, fully confirmed BALZER's thesis relative to Injections of Insoluble Mercury-compounds generally,—to wit: that *the Resorption of Mercury from Insoluble Injections proceeds rapidly at first, and more and more slowly later-on*,—THUS COMBINING THE ADVANTAGES OF BOTH ACUTE AND CHRONIC MERCURIALIZATION.

Methylal—$CH_2 \begin{cases} O\,CH_3 \\ O\,CH_3 \end{cases}$—is a very mobile, colorless liquid, boiling at 42° C [107.6 F]; of specific gravity 0.8551. It is *easily soluble* in Water, in Alcohol, in fatty and in ethereal Oils.

According to MAIRET and COMBEMALE (*Nouveaux Remèdes*, 1887; p. 133), it is administered *hypodermically* as a **Hypnotic**, or *externally* as a **Local Anesthetic**, or *internally* as an **Anodyne** in Neuralgias of the Digestive tract.

The latest researches by Prof. VON KRAFFT-EBING (*Therapeutische Monatshefte*, 1888; p. 55) have elicited the exceedingly beneficient **Sedative** action of subcutaneous injections of METHYLAL in *Delirium tremens*. He used 0.1 gramme [1½ grain] per injection, every 2 to 3 hours; and in successful curative treatment the daily number of injections applied by him amounted to at least seven.

For a *Liniment*, METHYLAL is mixed with 6 times its weight of EXPRESSED ALMOND OIL; for a *Dental Anodyne*, with 4 parts of COCA TINCTURE; for *Internal Medicine*, with 12 to 100 parts of WATER or SYRUP.

A *Lethal effect* is reached in dogs by the administration of one part of METHYLAL to 1000 of the animal's weight.

The sum total of the experimental results hitherto obtained with METHYLAL appears to bear sufficient inducement, warrant, and guide toward further special researches on its *Sedative and Hypnotic* action when applied subcutaneously, in *Asthenic* conditions of the *Central Nervous Complex.*

Myrtol is that portion of MYRTLE OIL (from the leaves of *Myrtus communis*) which distils between 160° and 170° C [320 and 338 F]. It is a limpid liquid, of aromatic, penetrant odor.

Prof. EICHHORST of ZÜRICH UNIVERSITY has recently commended MYRTOL as a reliable and energetic counter-agent to *Putrid processes in the Air-passages.*

Its Dose is of 0.3 gramme [4½ grains] every 2 hours; divided in two Gelatine capsules of 0.15 gramme each.

Phlorizin and **Diabetes.**—The Glucoside PHLORIZIN (also written "*Phloridzin*"; or "*Phlorrizin*"), which is found in the *bark* of *Apple-*, Pear-, Plum-, and Cherry-*trees*, especially in the *root-bark*, and to some extent also in the *leaves* of the Apple-tree, was physically described in the BULLETIN for April, 1888.

Prof. J. VON MERING, in 1885, discovered the fact that this Glucoside, given to dogs, causes an intensive *Mellituria*, without otherwise in the least altering the animal's general health.—Recently, VON MERING published the results of a new and more extended series of researches on the same topic (*Zeitschrift für Klinische Medizin*, 1888; p. 405). The relations hereby demonstrated as subsisting between PHLORIZIN and *Diabetes mellitus* are of remarkable interest; as will be seen from the following abstract:

> Dogs that were fed a long time on meat exclusively, showed *Dextrose in their urine* whenever PHLORIZIN had been given them, and the more so when the dose was increased. The character of the food remained without influence on this symptom; for when Carbo-hydrates were liberally given the animals, the quantity of Dextrose in the urine was not augmented.

But also in dogs which had received no food for 10 days, *Glucosuria* was induced by dosing them with PHLORIZIN. In one case the amount of Sugar in the urine was 46 grammes.—The same animal which had passed this enormous quantity of Sugar after a 10 days' fast, yielded another remarkable quantity after the same fast had been continued to 18 days' duration; that is, upon a 12 grammes' [185 grains'] dose of PHLORIZIN it urinated, within 48 hours, 37 grammes of Sugar—that is, over three times the quantity of the PHLORIZIN dose administered!—It must be borne in mind, in order to fully appreciate the remarkable character of this fact, *that, after a fast of the duration named, all the Muscles and the Liver must have lost their Glycogen.*

It had been assumed, hitherto, that **Artificial Diabetes** could NOT be induced *in an organism whose Liver was devoid of* GLYCOGEN. But VON MERING's researches, as above sketched, show that intensive *Mellituria* may be induced by doses of PHLORIZIN in an animal body whose Muscles and Liver are *both* totally devoid of GLYCOGEN.—He furthermore induced *Diabetes* by PHLORIZIN in geese *whose Liver had been wholly disconnected from the general circulation.*

Pyridine—C_5H_5N—is the initial member of the homologous series of so-called "*Pyro-Alkaloids*":

PYRIDINE, PICOLINE, LUTIDINE, COLLIDINE, PARVOLINE, CORIDINE, RUBIDINE, VIRIDINE,

which have the general formula "$C_nH_{2n-5}N$,"—and are hence considered as "Mono-methyl-pyridine," "Di-methyl-pyridine," "Tri-methyl-pyridine," etc.—They, or some of them, are always contained in the products of destructive distillation of Nitrogenous organic substances, and hence are found in *Coal-tar*, in *Peat-tar*, in *Dippel's Animal Oil*, in *Tobacco-smoke*, in *Empyreumatic Ammonia-water*, and the like.—PYRIDINE has also been obtained *synthetically* in small quantities.

PYRIDINE is a colorless, limpid liquid, of a peculiar, empyreumatic odor and sharp taste. Its specific gravity at 0°C [32 F] is 0.9858; its boiling-point is about 117° C (or between 116 and 118 [240.8–244.4 F]). It is *easily and clearly miscible with Water* at any ratio; the aqueous solution shows alkaline reaction. It is also *clearly miscible* with Alcohol, with Ether, with Benzin, and with fatty Oils. *When pure*, it is strongly *hygroscopic*,—readily attracting sufficient moisture

from the atmosphere to slightly increase its specific gravity and greatly depress its boiling-point.—It forms WELL CRYSTALLIZABLE SALTS, of which principally the following two have been employed for **Internal Medication:**

Pyridine Nitrate—$C_5H_5N.HNO_3$.—Slender, colorless needles, *easily soluble in Water;* less so in Alcohol.

Pyridine Sulphate—$(C_5H_5N)_2.SO_4H_2$.—Crystalline; *soluble at any ratio in Water and in Alcohol.*

PYRIDINE is to be kept in well-closed vessels, and *protected from daylight.*

—The **Physiological Action** of PYRIDINE was found by HANS DISTLER (*Dissertation*, Erlangen, 1887) to be *but very slightly toxic;* he himself having taken as much as 2 grammes [31 grains] *internally*, without experiencing any toxic symptoms. On rabbits, he found that as much as 1 part per 1000 of the animal's weight was required for producing *lethal action.* Death, in those cases, resulted by *Paralysis of the Respiration.*

HIS (*Archiv für experimentale Pathologie und Pharm.*, Band XXII; page 252), who experimented upon *the transformation of* PYRIDINE *in the animal economy*, found that dogs bore the dose of 1 gramme [15 grains] per day without any effect beside *slight Vomition and Diarrhea;* their urine thereupon was found to contain a Base, whose Hydrochlorate answered to the formula of "C_6H_8NCl"—corresponding, empirically, to that of PICOLINE HYDROCHLORATE.

—PENZHOLD found PYRIDINE to act as a **General Antiseptic** on *Mycelia.*

—GERMAIN-SÉE investigated the **Palliative** effect of PYRIDINE INHALATIONS in *Asthma.* He traced the well-known Anti-asthmatic effect of Tobacco-smoke, and more especially yet, of the smoke of the so-called "Anti-asthma Cigarettes," to the PYRIDINE BASES contained therein. The signal relief thus often obtained is, however, *properly confined* to cases of NERVOUS Asthma. (In the Asthmas of DEBILITY and HEART-DISEASE, the use of Pyridine should be *avoided!*)—It appears that, *taken by Inhalation*, PYRIDINE acts as a **Respiratory Sedative,**—*reducing both the direct and the reflective excitability* of the Respiration-centre.—The medicament, taken by the lungs, is *very rapidly absorbed*

into the system. After a few minutes' lapse, already, the presence of PYRIDINE in the urine can be shown.—The relief afforded by these Inhalations is *decided and prompt;* but it is, of course, *only of temporary duration*, so that the application has to be repeated when the trouble returns.—The *mode of exhibition* is as follows:—3–5 grammes [45–75 grains] of the PYRIDINE are left to evaporate spontaneously from a plate placed in the patient's room. At an atmospheric temperature of 20–25° C [68–77 F], the quantity stated will be evaporated in about an hour.

—E. ROSENTHAL (*Dissertation*, Erlangen, 1887) made a series of experiments with PYRIDINE as a **Topical Antiseptic** in *Diphtheria*. He found the best form of exhibition to be an *aqueous 10-% solution*, applied by cotton-wool Tampon held in angular nippers. Three to four applications per day, during 2–16 days, were used. The *percentage of cures* was 73.

—DE RENZI (*Rivista Clin. e Terap.*, 1887; No. 3) found PYRIDINE an excellent **"Heart-stimulant."** He exhibits it *internally*,—6–10 drops, in Water, per day; rising to 25 drops.

PYRIDINE, in the latter use, is *as well borne* as DIGITALIS, and *acts more efficaciously* in *Asystolic* conditions.

—RADEMAKER, of Louisville, Ky., considers PYRIDINE an excellent **Anti-Gonorrheic.** He claims to have obtained *cures* within 3–4 days by simple *Injections* of: Pyridine 0.1 gramme [1½ grain] to Water 30 grammes [1 fluidounce].—Here, he says, the PYRIDINE acts *antiseptically* on the local parasitic developments which characterize and create the *Gonorrhea*.

Resorcin (*Resorcinol*)—[*see Description in* BULLETIN *of June, 1888!*]—has been found by Dr. J. ANDERER (*Centralblatt für die Medizinischen Wissenschaften*, 1888; No. 42) to be *a Specific*,—probably the only one known so far,—in the supposedly incurable **Celoids** (Keloids).—This discovery has been confirmed by Priv. Med. Councillor Dr. NUSSBAUM.

The pain occasioned by *Celoids* vanishes on external application of CACAO-BUTTER containing 10 per cent. of RESORCIN. The *relief is complete and permanent.*

Safrol—$C_{10}H_{10}O_2$—the principal constituent of *Sassafras-oil*—has recently been lauded by Dr. C. L. DANA as an excellent **Anodyne** in *Acute or Sub-acute Rheumatism.*—His dose is 20–30 drops.

Simulo, Tincture.—(*Additional to* BULLETIN *of June, 1888:*)—Since the publication of HALE WHITE'S report on SIMULO, of which I gave an abstract, renewed investigations were made on this drug by Prof. Dr. EULENBURG, the results of which are given as follows:

1,—*He attaches no importance whatever to this drug as an* ANTI-HYSTERIC!

2,—As an **Anti-Epileptic,** *a certain degree of efficacy* was demonstrated in three or four cases; but this efficacy *fell short of that of the* BROMIDES, whenever these were administered in medium dose (6 to 8 grammes [90–125 grains] per day). In not a single instance was any superiority of the SIMULO over the BROMIDES apparent; and the dose of the former had to be *at least* 1½ to 2 teaspoons of the Tincture 2 or 3 times per day, in order to procure anything like a prompt effect.—Hence, Prof. E. concludes that SIMULO may only in exceptionally characterized cases prove a proper Succedaneum for the BROMIDES; and that it may perhaps sometimes be *eligible for combination* with them.

(There appears to be some likelihood, however, that *the active constituent* of SIMULO, when isolated, may prove an adequate competitor to the BROMIDES.)

Tannin, albuminated, is one of those modern forms for *Tannin internal medication*, which enjoy the advantages over SIMPLE TANNIN in powder or solution, of a *more agreeable taste*, and of a rapid resorption *without inconvenience to the stomach;* while the astringent action of the TANNIN *is of at least the same strength* as when administered pure!

The Dose of ALBUMINATED TANNIN is *twice* that of PURE TANNIN. It is exhibited in Shake-mixtures, which must, however, be consumed rapidly, as they do not keep over two days.

Trypsin in **Diphtheria** of Infants.—The following formula has been recommended for an *Antiseptic* and *Membrane-Solvent* mixture:

Trypsin 2 grammes [30 grains]; Soda Bicarbonate, the same; Mercury Bichloride (Corrosive Chloride) 0.015 gramme [¼ grain]; Glycerin 4 grammes [60 grains]; Rose-water 30 grammes [1 oz.].—Signed: "*For Spray Douche.*"

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Acetyl-phenyl-hydrazin, — $C_6H_5NH.NH.CH_3CO$,— also MISCALLED: **"Pyrodin".**—This new **Antipyretic** was first therapeutically described by Dr. DRESCHFELD (*Manchester Medical Society;* and *British Medical Journal*, 1888; p. 881). He states it to be an insipid powder, difficultly soluble in cold Water, and melting at 128.5° C [263.3 F]; *causing neither Nausea nor Vomit*, and *more prompt and energetic* in its Antipyretic action than either *Antipyrine or Phen-acetin.* The reduction of temperature in febrile conditions is said to result within 5 hours, and to last for 6–8 hours thereafter. Dr. D. rarely found more than one dose per 24 hours to be needed, as the reduction and subsequent partial recovery of temperature were followed by *a second reduction wave.* The reductions were *accompanied by perspiration, never by chills or collapse.* DRESCHFELD used the so-called "PYRODIN" in *Pneumonia*, *Typhus*, and *Hemicrania;* his Single Dose for *Children* was 0.2–0.25 gramme [3–4 grains], and for *Adults* 0.5–0.75 gramme [8–12 grains]. (*Excessive Doses* may produce *Hemoglobinuria*, and, thereby, *Icterus!*)—According to *later communications* by Dr. DRESCHFELD to Prof. LIEBREICH, however, the **Toxic Action** of "PYRODIN" *needs to be duly considered* in prescribing it. This second-thought has since been confirmed by LEPIN (*Lyon médic.*, 1888; No. 80).—E. GHILLANY (*Zeitschrift des Allgem. Oesterreich. Apoth.-Vereins*, 1889; p. 20) reports on the experimental use of "PYRODIN" in the General Hospital at Vienna, and he, in opposition to Dr. DRESCHFELD'S original statements, has VERY SMALL PRAISE for this medicament, as regarding both *promptness of action* and *freedom from accessory symptoms.*

—Now, the apparently irreconcilable contradiction between the several statements here quoted, and others,—BOTH FAVORABLE AND UNFAVORABLE,—seems to find a ready solution in view of the fact, WHICH HAS SINCE BEEN ASCERTAINED on good authority, that probably **No Definite Chemical Body** was employed in any of the rudimentary experiments on which these various reports are based,—**the so-called "Pyrodin,"** which was made by a British firm, and which was presumably used in these experiments, being **a Variable and Indeterminable Product,** consisting *in part* of TRUE ACETYL-PHENYL-HYDRAZIN, and *for the rest* of IMPURITIES or ACCESSORY PRODUCTS, the exact nature of which has not yet been ascertained.

But SO MUCH IS APPARENT from researches and comparisons already instituted, that THE VIRTUES AT FIRST CREDITED TO THE SO-CALLED "PYRODIN" *may likely be ascribable* principally or exclusively to its **Acetyl-phenyl-hydrazin** constituent, and *its later-ascertained Drawbacks* to FOREIGN MATTERS associated with this remedial nucleus.

—*Clinical tests* as to the correctness of these inferences can readily be made, as *I have recently prepared* the **Pure Acetyl-phenyl-hydrazin,** *exactly corresponding* to the above-stated formula: $C_6H_5NH.\ NH.\ CH_3CO$, and it will shortly be obtainable in the Drug-markets.

—[The *formula* of ACETYL-PHENYL-HYDRAZIN, as stated above, shows a marked relation to that of ANTIFEBRIN, —$C_6H_5NH.\ CH_3CO$,—differing from it but by the increment of one sole *Imido-group* (NH). Its derivative composition—from Phenyl-hydrazine with an Acetic-acid rest—relates it likewise to ANTITHERMIN,—$C_6H_5NH.\ N$ ([C. CH_3] [CH_2. CH_2. COOH]),—which is produced by the de-hydration of a combination of *Phenyl-hydrazine* with Levulinic (Beta-Aceto-propionic) Acid, a higher Homologue of Acet-acetic Acid.—Equally, the derivation of ANTIPYRINE (Phenyl-di-Methyl-pyrazolone)—C_6H_5N ([N. CH_3] [C. CH_3]. CH. CO),—from a Phenyl-hydrazine compound with Acet-acetic Ester, places that substance in relation with the subject of this article; and the analogy between ANTIFEBRIN, mentioned above, and its kin-compound PHENACETIN—$C_6H_4(OC_2H_5)NH.\ CH_3CO$ (differing by the substitution of an Oxy-Ethyl group [OC_2H_5] for a Hydrogen atom)—brings the latter-named Antipyretic also into the line of these chemically and therapeutically inter-related compounds.—Hence, the claim of ACETYL-PHENYL-HYDRAZIN, as a legitimate member of this extended Antipyretic family, to an *exact clinical test* of its powers—*when employed pure!*—rests on good presumptive evidence.]

Acid, Picric (*Picro-nitric*) in **Eczema.**—PICRIC ACID has recently been employed by CERASI (according to the *Gazzetta medica di Roma*), in the treatment of *Eczema impetiginosum*, with considerable success. Seven cases of this disease, affecting the face and scalp, were rapidly cured by local applications of the Acid. The ages of the patients were from 2 to 4 years.

Regarding the *mode of exhibition*, the following procedure has been approved:—The scabs, having been softened by oil, are removed; thereupon the diseased surfaces are covered with compresses soaked

in a 0.3–0.6-per-cent. solution of PICRIC ACID. From four to six applications suffice to largely reduce the capillary hyperæmia and the sero-pyoid exudation; and *a complete cure is readily effected.*

Benz-anilide (*Phenyl-benz-amide*) — $C_6H_5NH.COC_6H_5$. — This substance is constituted analogously to *Acet-anilide*,—being a derivative of Benzoic Acid and Aniline in precisely the same sense as the other is of Acetic Acid and Aniline.—Its *therapeutic qualities* are likewise similar to those of Acet-anilide.

E. KAHN has made a series of experiments with BENZ-ANILIDE in that direction, in the Infant Clinique of Prof. KOHL at Strassburg (*Wiener Medizinische Wochenschrift*, 1888; p. 1523). He found it *a powerful and well-borne* **Antipyretic.** Febrile temperatures were reduced by some degrees, within an hour, on as small a dose as 0.2 gramme [3 grains].

Prolonged BENZ-ANILIDE *medication* appears to dull the susceptibility of the organism to the drug; hence, *increasing doses* become necessary.

The **Caffeine Double Salts** (several of which *have been noticed* briefly in various Numbers of last year's BULLETIN!) have attained additional importance in the treatment of **Pulmonary diseases** through the recent researches of Dr. TE GEMPT (*Berliner Klinische Wochenschrift*, 1888; Nos. 25 and 26).

If properly administered in suitable doses, the effects are: Reduction of the *Respiration-rate;* Augmentation of the *Blood-pressure;* Diminution of *Temperature;* Improvement of the *Subjective condition.*

The favorable character of the effect of these salts is especially marked when, in Pulmonary affections, the indications demand a *Toning of the Heart-action and Respiration-centre.*

The CAFFEINE DOUBLE SALTS (MERCK) at present procurable in the Drug Trade are the following:

Caffeine and Ammonium,	**Citrate**	(54% Caffeine);
" " **Soda,**	**Hydrobromate**	(52% ");
" " **Sodium,**	**Benzoate**	(45.8% ");
" " "	**Cinnamate**	(62.5% ");
" " "	**Citrate**	(52.2% ");
" " "	**Salicylate**	(62.5% ").

Cannabine, Pure Alkaloid.—[*Additional to* BULLETIN *for June, 1888:*]—(The characterization of *this Alkaloid*, as an INNOCUOUS, PURELY HYPNOTIC Medicament, and a substance *entirely different* from the previously known *Resinoid* "CANNABIN," was given as above quoted.)

RAFFAELE VALIERI, of Naples, has now (as reported in the *Wiener Medizinische Presse*, 1888; No 41) experimented with the PURE ALKALOID CANNABINE in several cases of *Morbus Basedowii*, and obtained excellent results, after all other remedies had proved unavailing. He uses 0.3 gramme [5 grains] of CANNABINE ALKALOID *per diem*,—either divided into 5 Pills, or in mixture with Syrup and Water.

Curare (also spelled: "*Curara*," "*Woorara*," "*Wourari*," "*Wouarali*," "*Urari*") is an arrow-poison used by the natives of several South-American countries, and is prepared by them from various species of *Strychnos*, particularly *S. toxifera*.

It comes in the form of a brownish-black, solid Extract, of bitter taste. The greater part of this is soluble in cold Water, and the aqueous solution contains most of the active principles of the drug.

CURARE exercises *no marked therapeutic action through the stomach.*—It is, however, used SUBCUTANEOUSLY as a **Muscular Paralytic**, in *Tetanus*, *Hydrophobia*, etc.

The DOSAGE of CURARE is *a delicate point* of practice; for *the various toxic strengths* of the native preparations render a uniform direction impossible at the present day.—It is, therefore, *advisable either to test the strength* of the drug, *when not* already known, by *experiments on animals*, before determining the human dose; *or, at least, to proceed cautiously from a stated minimum* to gradually increased doses.

Of the STRONGEST VARIETIES, the *Lethal Dose*, *hypodermatically*, for a frog is $^1/_{10}$ milligramme [$^1/_{650}$ grain]; and for a rabbit, 1 milligramme [$^1/_{65}$ grain], in aqueous solutions. Of THESE VARIETIES, the *Human Dose* may be assumed at 5 milligrammes [$^1/_{13}$ grain],—*being ½ cubic centimetre* [8 minims] *of a 1-% aqueous solution*, administered by hypodermic injection.

THERE ARE, HOWEVER, VARIETIES of which *the tenfold amount may be needed;* that is, where 1 milligramme may be required, hypodermati-

cally, to kill a frog, and 10 milligrammes for a rabbit.—With these, the above-indicated solution for the Human Dose would have to be made *proportionately stronger*,—say up to 10 per cent. instead of 1%.—OFFENBERG frequently used solutions of 5 per cent.,—injecting 1 cub. cm. [16 minims] thereof into the Human system at a time; thus using 50 milligrammes [$^{10}/_{13}$ grain] of the drug per injection. Of VERY WEAK VARIETIES, even 100 milligrammes [1½ grains], or more, of the drug were used. In one case, Offenberg injected a total of 0.22 gramme [3⅓ grains] of CURARE at a time.

—A practical and safe way of proceeding with the HUMAN SUBCUTANEOUS INJECTIONS is as follows:—Prepare a 1-% *aqueous solution* of CURARE; if preferred, let the menstruum contain an admixture of GLYCERIN or of a very little HYDROCHLORIC ACID. Filter the solution before using. If the strength of the drug has not previously been tested or tried, BEGIN by injecting *from one-fifth to one-half a hypodermic syringeful;* GRADUALLY AND CAUTIOUSLY INCREASING quantity of injection or strength of solution, or both, as may seem to be needed, in subsequent injections, *until the desired effect be attained.*—(INTERNAL administration is, as above indicated, useless.)

Curarine.—**Alkaloid** from, and *active principle of*, CURARE (see above!).—Not to be confounded with the *therapeutically inert Alkaloid* "**Curine,**" which likewise occurs in CURARE!

Prepared according to Prof. BÖHM'S method, *the Active Alkaloid* CURARINE appears as a yellowish-brown, amorphous, hygroscopic powder, of intensively bitter taste. It is *easily soluble* in Water and in Alcohol; insoluble in Ether. It shows no perceptible alkaline reaction. (Its alcoholic solution presents a slight fluorescence.)—According to Prof. BÖHM, it forms *no true Salts*, but decomposes on being heated with mineral acids,—forming a crystalline derivative which has not yet been investigated.—*Concentrated* Sulphuric Acid dissolves CURARINE, producing a crimson color, which, on the addition of a little Potassium Bichromate, passes into a bluish tint.

The **Therapeutic Uses** and FORM OF EXHIBITION are *the same* for CURARINE as for CURARE (above!).—According to Prof. BÖHM, the *Lethal Dose* for rabbits is 35 parts per 100,000,000 of the animal's weight

[0.35 milligramme per kilogramme].—*The strength of this preparation* (CURARINE) *may vary*, similarly to that of CURARE,—according to the origin of the Crude Drug from which it is prepared. Hence, it is *advisable to test it on animals* before determining the Dose for Man.

Eschscholtzia californica (*California Poppy*).—BARDET and ADRIAN (*Nouveaux Remèdes*, 1888; p. 530) succeeded in isolating from aqueous infusion of this Papaveraceous plant, which has long been known as possessing Narcotic properties, a small portion of MORPHINE, and, besides, an unknown Glucoside and a second Basic substance, which latter is probably a fractional derivative of the Glucoside. (Hitherto, MORPHINE had not been found outside of the Genus *Papaver* proper.)

A special indication for the *therapeutic use* of ESCHSCHOLTZIA C. appears to be given in those cases where a **Moderate Narcotic** effect is to be desired. It may be expected that the drug will obtain a wide application, for this reason, in **Infant Practice,** where the administration of the stronger OPIATES is so often found to entail sad consequences.

So far, the ALCOHOLIC and the AQUEOUS EXTRACT of this plant have principally been used. The *daily doses* thereof ran from 2.5 to 10 grammes [38–154 grains].—Dr. TER-ZAKARIANTZ (in *Semaine Médicale*, 1888; No. 52) recommends the following formulas:

1.—*Alcoholic* Extract Eschscholtzia calif. 2.5–10 grammes [38–154 grains]; Best Rum 30 grammes [1 oz.]; Syrup Gum Arabic, *same*.

2.—*Aqueous* Extract Eschscholtzia calif. 3–12 grammes [46–185 grains]; Infusion Pectoral Tea 100 grammes [3¼ oz.]; Syrup Gum Arabic 40 grammes [1⅓ oz.].

3.—*Aqueous* Extract Eschscholtzia calif. 1 part by weight; Syrup (simple) 8 parts.—One to four tablespoonfuls per day.

4.—*Alcoholic or Aqueous* Extract Eschscholtzia calif. about 20 grammes [310 grains]; Powdered Licorice-root, sufficient to make 40 pills.—Five to fifteen pills per day.

Ether, Ethylic (so-called **"Sulphuric Ether"**; or, simply, **"Ether"**)—**for Analyses.**—This grade of ETHER *is re-distilled over Sodium Metal*, and, consequently, *is entirely free* from ACID, from WATER,

and from ALCOHOL.—Specific gravity 0.718–0.720; boiling-point about 34–36° C [or about 93–97° F].

This grade of ETHER is intended for the *finest and most exact* kinds of Laboratory work; for *ordinary* analytical purposes a chemically pure ETHER of spec. grav. 0.720–0.722 (corresponding herein to the *Æther fortior* of the U.-S. Pharmacopœia), will suffice.

—*All such* high grades of ETHER, destined for analytical purposes, *must be kept protected from daylight.*

Lithium Salicylate is pronounced by the Parisian scientist VULPIAN to be **of more searching effect than Sodium Salicylate,** in *Gout* and in *Acute Articular Rheumatism.* He maintains that the Lithium Salt is capable of *consummating the action* of the Sodium Salt, —*removing the last traces* of febrile irritation, in cases where this end was not attainable through the Sodium Salicylate.—In *Chronic Rheumatisms*, and particularly in Rheumatic affections of the *Tendons*, the LITHIUM SALICYLATE also shows the better action of the two Salts.

The *usual medium dose* is, by the above-named authority, placed appreciably higher than current works state it; to wit, at 4 grammes [60 grains], which may without scruple be increased to 5 grammes [75 grains]. It is not until the dose *exceeds* the latter quantity, that any unpleasant reaction on the organism has been found to occur.

Mercur-Alanine (**Mercury Alpha-Amido-propionate** [**Lact-amate**]) was first extensively tested in Therapy by WOLF, of Strassburg, and has recently been especially applied in **Syphilis** by DE LUCA.—It is administered *subcutaneously* in the form of a solution of 4–8–10 milligrammes [$^1/_{16}$–$^1/_8$–$^1/_6$ grain] of the Salt in 1 cubic centimetre [16 minims] of Water.

—(MERCUR-ALANINE is also administered *internally*, in like doses as most other mild Mercury Salts; but, in *this* mode of exhibition, it seems to possess *no advantages* over MERCURY TANNATE or PHENATE.)

Naphthol, Beta-, (also called: *Iso-Naphthol*).—BOUCHARD'S recommendation of BETA-NAPHTHOL, as being a *very slightly toxic, but efficacious*, **Intestinal Disinfectant,** has now been supplemented in another direction by the experiments of REVERDIN (*Société Médicale de*

la Suisse romande) who subjected this substance to a series of trials as a **Surgical Antiseptic.**—REVERDIN's statements are quite encouraging; for he obtained a *complete healing result* "*per primam intentionem*" in almost each case treated.—In Surgical uses the BETA-NAPHTHOL is exhibited either in *Powder*, or in 10–15-% *Wadding*, which is prepared by sterilizing Cotton Wadding at 130° C [266 F], and then impregnating it with an *Ethereal solution* of BETA-NAPHTHOL.

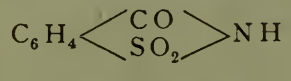
Dr. RUAULT has further employed BETA-NAPHTHOL WATER with good effect in **Ozena** (*Ozæna*).—The mixture herefor is prepared by dissolving 125 parts, by weight, of BETA-NAPHTHOL in 88 of Alcohol, and stirring a dessertspoonful of this solution into a quart of Water. —The disagreeable sensation at first caused by the application of this mixture ceases to recur after a few more applications.

"Pyrofuscin" is the name given by Prof. P. F. REINSCH to a substance discovered by him in various kinds of Bituminous Coal (in which, however, it occurs in very variable proportions), and applied by him in his new process of *Leather-Tanning*, in which it acts with exceeding energy and rapidity. The cellular structure of animal skins becomes converted into proper and durable Leather after a very brief immersion in a PYROFUSCIN solution.

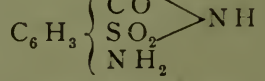
PYROFUSCIN appears to belong, in its chemical relations, to the HUMIN (or ULMIN) group. It is separated from the Coal by boiling with Alkaline solutions. It is a weak acid.

In Alkaline solution, it develops a remarkably strong **Antiseptic** action.

Saccharin-amide (*rational name:* **para-Amido-benzoyl-sulphinide**).—This is a new *Non-carb-hydratic Sweetener*, closely related to SACCHARIN (*see* BULLETIN *for June, 1888*), as will be evident from the respective formulas:



(Benzoyl-sulphinide) [Saccharin];



(para-Amido-benzoyl-sulphinide) [Saccharin-amide].

Its discoverer is A. NOYER.—SACCHARIN-AMIDE is poorly soluble in cold Water. A solution of it in *hot Water* exhibits a deep-blue fluorescence, and has an intensively and persistently sweet taste.

STRAY ITEMS.

No. 1.

HYOSCINE.

Hyoscine;—and **Pioneers in Chemical and Therapeutic Research.**

The name "Hyoscine" was first **proposed** by HÖHN and REICHARDT (*Annalen der Chemie und Pharmacie*, Vol. 157 ; page 98) as a designation, supposed to be proper, *for the basic decomposition-product of* HYOSCYAMINE.

Prof. Dr. A. LADENBURG, of KIEL UNIVERSITY, — in *Berliner Chemische Berichte*, 1880; p. 607,—thereupon demonstrated that supposedly new product to be identical with the previously-known *derived Alkaloid* TROPINE ; and, in consequence hereof, the newly proposed name of "Hyoscine" for that substance was dropped. On April 30th, **1880**, page 909 of the *Chemische Berichte* contained an article by Prof. LADENBURG, reporting on the existence of **a Second Alkaloid** in *Hyoscyamus niger*, which that chemist had **discovered** in, and succeeded in isolating from, a series of preparations furnished him by E. MERCK.

The results of an exact investigation of the physical and chemical properties of that **Second Hyoscyamus Alkaloid** were described by its above-named discoverer and investigator, A. LADENBURG, in the *Berichte* of June 24th, **1880 ;** page 1549. This report culminated in positively demonstrating the existence of that SECOND ALKALOID in *Hyoscyamus*,—as pre-formed, and independent of HYOSCYAMINE,—and in giving to it the empirical name **HYOSCINE**, which name was thenceforth accepted for it by all chemists.

—Then, in **1881**, appeared the following reports on the **Physiological and Therapeutic properties** of HYOSCINE :

1. Prof. EDLESSEN and Dr. ILLINGS : "Ueber die therapeutische Verwendung des HYOSCINUM HYDROCHLORICUM und HYDROJODICUM (LADENBURG)." — *Centralblatt für die Medizinischen Wissenschaften*, 1881 ; p. 416.

2. Dr. K. GNAUCK : "Ueber die Wirkung des HYOSCINS." —*Same*, 1881 ; p. 801.

(The last-named report already mentions the efficacy of HYOSCINE in **Psychiatric** medication.)

In **1883** and **'84**, there appeared in public print the following **additional** notable essays on the same subject :

3. PH. J. A. CLAUSSEN : "Die Wirkung des HYOSCINUM HYDROJODICUM und HYDROBROMICUM, im Vergleich mit denen des ATROPIN und des EXTRACT. HYOSCYAMI."—*Inaugural Dissertation.* 42 pages. Kiel, 1883.

4. HAVER DROEZE (Dordrecht) : "Eenige anteekeningen over waargenomen werking van HYDROJODAS HYOSCINI." — *Weekblad van het Neederl. Tijdschr. voor Geneeskd.*, 1883 ; No. 36, p. 631.

5. O. FRÄNTZEL : "Ueber die Wirkung des HYOSCINS gegen die Nachtschweisse der Phthisiker." —*Charité-Annalen*, 1883 ; p. 301.

6. C. W. TANGEMAN : "ATROPINE and SIMILAR bodies, in general and special practice." — *Therapeutic Gazette*, 1884 ; VIII ; June, p. 247.

7. A. LADENBURG and C. F. ROTH : "Ueber das HYOSCIN." — *Berichte der Deutschen Chemischen Gesellschaft*, 1884 ; XVII, p. 181.

8. KOBERT likewise discussed HYOSCINE in his *Jahresbericht der Pharmacie und Therapie*, 1884 ; p. 191.—He there says :

> "It is desirable that **Psychiaters** repeat, with HYOSCINE, experiments they have made
> "with HYOSCYAMINE; for, the effects of that highly interesting Alkaloid being widely differ-
> "ent from those of the other Tropeines, it would not surprise us to learn that it exercises
> "remedial powers in quite a different set of complaints."

—Then, in **1885**, appeared a **specially American series** of researches, led by the labors of Prof. Dr. H. C. WOOD,—as follows :

1. H. C. WOOD : "HYOSCINE ; its physiological and therapeutical action." — *Therapeutic Gazette*, 1885 ; Jan. 15th.

2. THE SAME and CH. J. HARD : "HYDROBROMATE OF HYOSCINE as a Hypnotic in Insanity." — *Same*, 1885 ; Feb. 15th, p. 107.

3. H. C. WOOD : "A partial study of MERCK'S HYOSCINE." —*Same*, 1885 ; Oct. 15th, p. 649.

4. JUDSON B. ANDREWS (Buffalo) : "Report on new remedies—HYOSCINE HYDROBROMATE." — *American Journal of Insanity*, 1885 ; Oct., p. 165.

5. HENRY M. WETHERILL : "HYOSCINE HYDROBROMATE." — *Philadelphia Medical Times*, 1885 ; Dec. 26th, p. 537.

6. PETERSON and CH. LANGDON : "HYDROBROMATE OF HYOSCINE ; its use in cases of Insanity." —*Medical Record*, New York, 1885.

—(*A Leaf from my Book of Record.*—E. M.)

MERCK'S BULLETIN

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Acid, Embelic—$C_9 H_{14} O_2$—has been discovered by H. WARDEN (*Pharmaceutical Journal and Transactions*, 1888; Oct. 20, p. 305) in the berries of *Embelia ribes* [MYRSINEÆ].

EMBELIC ACID is a definitely crystallized solid, melting into a reddish fluid at 139.5–140° C [283–284 F], and decomposing at 155° C [311 F]. It is well soluble in Alcohol; not in Water. It readily forms SALTS with Alkalis.

One of these Salts, the **Ammonium Embelate,** forming red needles, is an excellent **Taenifuge,** reported to be *efficacious where other Anthelmintics have failed!*

The *dose* of this Salt for *Children* is stated at 0.18 gramme [2¾ grains]; for *Adults*, 0.36 gramme [5½ grains], or more.—It is best administered in mixture with a little HONEY or SYRUP, and *preceded or followed* by a dose of CASTOR-OIL.

—EMBELIC ACID has the advantage, over other Anthelmintics, of being *wholly tasteless.*

Apocynum cannabinum (*Canada Hemp; American "Indian Hemp"*), **Aqueous Extract;** *from the root.*—The plant is known as a powerful **Emetico-Cathartic** and **Diuretic** in *Dropsy.*—Its AQUEOUS EXTRACT is administered, principally with regard to the *Purgative* effect, three times per day, in doses of 0.2–0.26 gramme [3–4 grains]. The *drastic manner of action* of this drug should, however, command caution.

Borneol, artificial,—$C_{10} H_{18} O$,—as obtained by Armstrong and Fielden from *Colophony*, is *chemically undistinguishable* (so far) from the **Native** or **True Borneol,** or **Borneo-camphor.** Its alcoholic solution, however, is *optically inactive*, that is, incapable of rotating polarized light; which circumstance is at present the only known one distinguishing it from the Natural Camphor Borneol, whose solution is dextro-rotatory.

BORNEOL resembles the COMMON (OFFICINAL, or LAUREL) CAMPHOR in its appearance in bulk; it consists of leafy, white crystals, and has a camphorous and terebinthine odor. In dense crystalline pieces, it is *heavier* than Water; while Common Camphor is lighter. It melts at 199° C [390.2 F].

Borneol, administered to frogs, acts like Laurel Camphor in *reducing the pulse-rate*, but making the pulse fuller at the same time. According to Ralph Stockman, however, it induces, besides, a *paralyzation of the Pneumo-gastric Nerve*, which has not been noticed after the Common Camphor.

Butyl-chloral Hydrate—$C_4H_5Cl_3O$ + aq.—(*Normal Tri-chlor-butyl-aldehyd Hydrate*)—was, for some years after its discovery, in 1870, and still is largely, known by the name of "**Croton-chloral Hydrate,**" which, however, is really a *misnomer* in this instance, as it properly applies to a substance of the formula "$C_4H_3Cl_3O$ + aq."

Butyl-chloral Hydrate is well enough known as an **Anodyne** in those *Trigeminal Neuralgias* where the painful condition is not of a chronic nature, and in *Facial Rheumatisms.*—It has, moreover, been found very eligible in *those* **Dental pains** which are caused by *Inflammation of the Pulpa*, or by *Periostitis.* It is likewise quite efficacious in relieving the disagreeable *sensation of pressure* attaching to *freshly-filled teeth.*

Its unpleasant *taste* is best masked in the following—the "improved Liebreich"—formula:

> Butyl-chloral Hydrate 2–3–5 grammes [30–45–75 grains]; Alcohol 10 grammes [3 fluidrams]; Glycerin 20 grammes [4 fluidrams]; Distilled Water 120 grammes [4 fluidounces].—*Three to four Tablespoonfuls at a time.*

Creatine (*Methyl-glyco-cyamine*),—$[C{=}\overset{NH_2}{\underset{N(CH_3).\,CH_2.\,COOH}{NH}}$, *or* $C_4H_9N_3O_2]$,—in the *anhydrous* state, forms an opaque, white solid, inodorous, and of a somewhat bitterish-acrid taste. Its *Mono-hydrate* appears in limpid prisms, which lose their crystal-water at 100° C [212 F].—Creatine is soluble in about 70 parts Water; almost insoluble in Absolute Alcohol.

Creatine is one of those constituents of Meat-soups and Meat-extracts, which impart to these preparations their appetizing taste and their stimulating effect on the Heart and general Muscular action.

Th. J. Mays demonstrated, some time ago (*Practitioner*, 1887; Oct.), that Creatine solutions as weak as 1:2000 are capable of

re-animating a frog's *Heart* which has been fatigued and finally arrested by the administration of Sodium Chloride.

More recently (*Chemiker-Zeitung*, 1888; p. 1662), Prof. KOBERT, of Dorpat University, published a very favorable opinion on the physiological action of CREATINE.—He recommends its use, in doses of 0.1 gramme [1½ grain], four to six times per day, as being *of undoubted value* as an **Excitant of Muscular Action** *in Atonic conditions* of the general Muscular system, of the Heart, and of the Digestive organs. —It is administered in form of *Powder*, placed *dry* on the tongue, and followed by a draught of Water.

—(*Similar effects* are produced by LIEBIG'S MEAT-EXTRACT *deprived of its* SODIUM CHLORIDE;—but the *Colloid constituents* of the Extract are *obstacles to good action* in *Gastro-Intestinal* complaints.)

Ethyl Bromide and **Ethylene Bromide.**—In recent times, since ETHYL BROMIDE has gained renewed favor as an *Anesthetic in Light Surgical Practice*, *Obstetrics*, *etc.*, (see BULLETIN for *June*, *1888!*), there have been several cases where ETHYLENE BROMIDE was *erroneously administered* in its stead,—the similarity of the names having led to either a false prescription or a false dispensation.

Dr. HIRSCH (*Therapeutische Monatshefte*, 1888; p. 556) relates details of such a case, which demonstrate the serious character of that error. He had ordered about 100 grammes of ETHYL BROMIDE for an operation. The medicament being applied, the expected Analgesy and Unconsciousness *failed* to set-in; in their place Vomition, Mortal pallor, Cerebral pain, and Tinnitus aurium arose.—Thereupon the supposed Anesthetic was examined, and found to be BROMIDE OF ETHYLENE (*not of* ETHYL!).

—The *very favorable reports* by Dr. J. ASCH, as quoted in the BULLETIN of June, 1888, on the merits of **Pure Ethyl Bromide** for *Anesthesia*, have found full confirmation by the recent labors of Dr. LEO SZUMANN (*Therapeutische Monatshefte*, 1888; April and May); who, however, also raises a warning voice against any confusion of it with ETHYLENE BROMIDE.

—**The desirable Anesthetic** is variously known by the names of: 1) *Bromide of Ethyl*, 2) *Bromino-Ethyl*, 3) *Mono-brom-ethane*, 4) *Hydro-*

bromic Ether, 5) *Æthyl bromidum* [U. S.], 6) *Æther bromatus* or *hydrobromicus* [Germ.], 7) *Éther bromhydrique* [Gall.];—all of which signify the compound: C_2H_5Br, which boils at 38–39° C [100.4–102.2 F]. (When *properly made* **for medicinal purposes,** it is evolved by distillation from Potassium Bromide, Alcohol and Sulphuric Acid, and subjected to subsequent purifications.)

The other substance above discussed—known as BROMIDE (or BI-BROMIDE) OF ETHYLENE (*Æthyleni bromidum*, or *bi-bromidum*), and represented by the empiric formula $C_2H_4Br_2$, which characterizes it as a *Di-brom-ethane*—is recognized most readily by *its high boiling-point* of 131° C [267.8 F].—IT HAS NO ANESTHETIC POWERS WHATEVER!

Gratiolin,—*stated as* $C_{20}H_{34}O_7$,—is one of the two *natural* GLUCOSIDES occurring in *Gratiola officinalis* (Hedge-hyssop),—the other being GRATIOSOLIN.—[Their fractional *derivatives*—by treatment with mineral acids, etc.,—include: GRATIOLETIN, GRATIOLERETIN; GRATIOSOLETIN (itself a glucoside), GRATIOSOLERETIN, and HYDRO-GRATIOSOLERETIN.—GRATIOLACRIN is still a third *natural* constituent of the same plant.—These are mentioned here, in order to prevent confusions arising from the similarity of names.]

GRATIOLIN, as prepared by MERCK, appears in lustrous, brown scales, of bitter taste; *easily soluble* in Water and somewhat less readily in Alcohol.

The *Therapeutic Action* of this Glucoside has not yet been determined.—The HERBA GRATIOLÆ was formerly officinal in the character of a *Drastic Purgative;* GRATIOLIN, being its active constituent, probably possesses like properties in an intensified degree.

Hamamelis virginica (*Witch-hazel*), and **Hydrastis canadensis** (*Golden Seal*),— **Fluid Extracts.**

Both these extracts were used by Dr. KÖNIGER (*Therapeutische Monatshefte*, 1888; Nov.) with excellent effect in **Pulmonary Hemorrhages.**

In *periodically recurrent Hemorrhages*, the HYDRASTIS preparation was successfully given as a **Prophylactic,** to avert the threatening attack,—similarly as in *Hypermenorrhea* (over-abundance of Menstruation).

—In addition hereto, *both* Extracts were found to act as beneficent **Tonics,** and to *stimulate the appetite for food.*

—The *doses* were 20–30 drops,—from three times per day, up to once hourly.

Lantanine is an *Alkaloid* recently discovered by BONIZA and NEGRITA (*Chemisches Centralblatt*, 1888; p. 1620) in the well-known plant *Lantana brasiliensis*, which the native Peruvians call "Yerba Sagrada."

LANTANINE acts as an **Antipyretic** in *Febrile conditions*, similarly to QUININE.—It is *well borne* by even very weak stomachs, and has proved *of excellent efficacy in Intermittent Fevers which had resisted* QUININE.

LANTANINE may be given within the limits of 0.1 to 2.0 grammes [1½–30 grains] *per diem;* it is best administered *immediately after* a Febrile attack, whose return it then usually prevents.

Lupanine—$C_{15}H_{25}N_2O$—is a NEW ALKALOID, discovered by MAX HAGEN in the seeds of *Lupinus angustifolius* (Narrow-leafed Lupin).—[See *Archiv der Pharmacie*, XXXII; p. 989.]—It must not be confounded with the *two older Alkaloids:* LUPININE and LUPINIDINE, found in *Lupinus luteus;* nor with the Lupin-*Glucoside* and its *Derivative:* LUPININ, and LUPIGENIN.

LUPANINE, the new Alkaloid, is of honey consistency, light yellow color with green fluorescence, strong alkaline reaction, bitter taste, and a Conium odor.

—(Its therapeutic or physiologic action is, as yet, but imperfectly understood.)

Menthol is given **internally** by Dr. C. L. DANA as an *Anodyne* in *Hemicrania* and in *Neuralgias.*—His doses are from 0.3 to 0.6 gramme [5–10 grains], taken in *hot* Water.

Sodium "Chloro-borite" has recently been recommended by Dr. R. RÜGER (*Convention of German Naturalists* at Cologne; *Chemiker-Zeitung*, 1888; p. 1320) as a **Food-Preservative** or **Anti-Zymotic**), when used in the proportion of *one part*, by weight, to *two hundred* of the article to be preserved.—Its Antiseptic action is caused by a slow, spontaneous elimination of CHLORINE from the salt.

Solanine—whose formula has not yet been determined with certainty (a number of various statements existing for it)—is a *Basic Glucoside;* that is, it is capable both of forming true Salts with Acids, and also of being fractionated into a Glucose and another, peculiarly characterized substance ("*Solanidine*").—SOLANINE is contained in widely different species of *Solanum*, but is obtained chiefly from the sprouts of the Potato (*Solanum tuberosum*). It forms colorless, lustrous, fine needles, melting at 235° C [455 F]. It is nearly insoluble in Water, Ether, and Benzene; little soluble in cold Alcohol, easily so in hot. Its taste is slightly bitter, somewhat pungent.

According to recent researches by Dr. J. SARDAS (*Bulletin gén. thérap.*, 1888; May 30) SOLANINE is an excellent **Neurotic Sedative,** more efficacious in long-standing *Neuralgias*, and especially so when *Neuritis* is present, than either ANTIFEBRIN or ANTIPYRINE; it calms the *Gastric* and the lightning-like *Tabetic* pains, and is pre-eminently adapted for assuaging *Locomotor excitation.*

In INTERNAL doses of 0.025–0.05 gramme [⅜–¾ grain] *per day*, according to Dr. SARDAS, it very rapidly reduces and effaces the Tremor of *Sclerosis* "*en plaques*," the morbid *Reflex excitability*, and the *Epileptoid tremor.* (Its action is, however, less prompt whenever the symptoms of sentient or motor Nerve-affection are dependent on some anatomic lesion!)

—(The SUBCUTANEOUS administration of the SOLANINE **Salts** [as, for instance, of the HYDROCHLORATE], is easily effected, as they are *readily soluble in Water.*—But *this use of them has been discountenanced* already by ADRIAN in 1887, for the reason that even the *Normal Salts* of Solanine [which is but a weak base] are apt to show decided *Acid action*, producing irritation and pain.)

—The TOXIC ACTION of the PURE SOLANINE GLUCOSIDE, taken *internally*, has, however, been much overestimated! *Single* doses of 5 centigrammes [¾ grain], given 3–4 times per day, and gradually increasing to as high as 30 centigrammes [4½ grains], are now quite usual; the rate of increase may be such as to run up to a *daily total* of 40–50 centigrammes [6–7½ grains] within three or four days after commencing SOLANINE medication.—It may conveniently be exhibited in *Pills* or in *Wafers*, containing 1–5 cgm. [⅙–¾ grain] each.—The dose is taken *with a meal*, and followed by a draught of Sugared Water.

Urechites suberecta, and its **Toxic principles.**—The above-named APOCYNEA, indigenous to the island of Jamaica, was investigated for its toxic constituents as early as 1878, when J. BOWREY extracted from it two extremely poisonous *Glucosides:* URECHITIN—$C_{28}H_{42}O_8$,—and URECHITOXIN, whose composition is supposed to be $C_{13}H_{20}O_5$.—*The former* appears in needles of intensively bitter taste, almost insoluble in Water, easily soluble in hot Alcohol; *the latter* is more readily soluble in Water, also bitter, and presents a crystalline form. The latter Glucoside may be derived from the former, or may be obtained directly from *Urechites-suberecta* leaves dried at 100° C.

MINKIEWICZ, at Dorpat University, (*Inaugural Dissertation*, Dorpat; 1888) has recently isolated from the same plant also an **Amorphous Glucoside** and an **Acid Resin,** both of which he found to be *eminently toxic*,—the *lethal* dose for cats being from 6 to 1 part per 1,000,000 of the animal's weight.

The URECHITES POISONS are **Heart-motor Excitants;** they kill finally by *Heart-arrest;* they at first induce a central and peripheral excitation in the *Vagus*,—subsequently paralyzing the same. The *Blood-pressure* is at first augmented by increased Heart-action; afterwards reduced by subsequent slowing-down of the Heart-beat and diminution of the Heart's contractile energy. The *Central Nervous System* is influenced paralytically.—The *accessory effects* of the URECHITES POISONS in small doses are those of a *Central Vomitive*, a *Ptysmagogue*, and a *Peristaltic Stimulant.*

The intensively toxic character of these substances precludes, as yet, any speculation as to the probability of their being successfully introduced into general THERAPEUTICS. However, from a specifically *toxicologic* point of view, they offer high interest,—URECHITES appearing to be closely related in its effects to STROPHANTHUS; and being, likewise, an **Antidote to Curare.**

Viburnum; and **Viburnin.**—The bark of *Viburnum prunifolium* (Black Haw) has since some time been valued, especially by American physicians, as containing a remedial agent serviceable in various **Uterine Troubles;** but *exact reports* on its mode of action in this direction, on its dosage, the nature of its active principle, etc., were largely felt to be wanting. A recent report on this drug is that of Dr. DEBIERRE (*Nouveaux remèdes*, 1888; p. 396).

Dr. D. highly lauds the FLUID EXTRACT of VIBURNUM in *Premature Labor*, *Habitual Miscarriage*, and *Uterine Hemorrhage.* He found a dose of 2–10 grammes (30 grains to 2½ drams) *per day* to be appropriate,—administering half a teaspoonful from once a day to three-hourly. It is administered with the best effect during the 4 days *next preceding* AND the 4 days *next succeeding* the usual or calculated commencement of the menstrual period.—When it appears needful to avoid the unpleasant odor of the drug, however, he prefers to use the SOFT EXTRACT, exhibited in *Pills*,—the *daily dose* being 0.25 to 0.60 gramme [4–9 grains].—(In formulating this dose, the Doctor must have had a SOFT EXTRACT of pretty strong concentration in view; as his dose limits *here* are *only one-eighth to one-sixteenth* of those indicated for the FLUID EXTRACT.)

The TINCTURE of BLACK HAW was also used by Dr. D., at the rate of 20–25 drops every three hours.

—The *Active Principle* contained in the Bark: VIBURNIN, is stated by Dr. D. as being given by him in doses of 0.05–0.15 gramme [¾–2¼ grains].

(This determination of the medicinal powers of **Viburnin,** and of their *kind* and *degree*, is a matter of especial interest to Clinical practitioners.)

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☞ ***This Cover*** (consisting of the *first* and the *last* leaf of this "Bulletin") *is intended only to serve the temporary purpose of preserving this Number until the completion of the year's Volume;* when it may be taken off and replaced by a complete yearly Index and Title-page, to be furnished with the December Number, for the purpose of binding the whole into a continuous book.

NOTICE.

☞ During the year 1889 there will appear in "MERCK'S BULLETIN" a newly compiled

TABLE
OF
MAXIMAL DOSES
(SINGLE AND DAILY),

—regarding most especially the NEWER REMEDIES, *not hitherto tabled* in the Pharmacopœias or Dispensatories.

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Acid, Hydro-cinnamic (*Homo-toluic ; Benzyl-acetic ; Beta-Phenyl-propionic*),—$C_6H_5.CH_2.CH_2.COOH$,$=C_9H_{10}O_2$.— Acicular, reddish-white crystals; poorly soluble in Water; soluble in 6 parts of Alcohol. Slightly acid reaction. The alcoholic solution has a pleasant acidulous taste and an aromatic odor, which spreads through the surrounding atmosphere.

Some time ago, Drs. KLEIN and LINGARD had achieved remarkable successes with HYDRO-CINNAMIC ACID in the destruction of the Virus of **Pulmonary Tuberculosis.** In consequence hereof, Dr. C. E. WILLIAMS was induced to institute clinical experiments on Phthisical cases (*Practitioner*, 1889; Feb., p. 100).—He used the *Alcoholic solution*, as above indicated; beginning with a dose of 10 minims in an ounce of Water [0.6 cub. cm. in 30 grammes],—rising, generally, to 20 minims in 2 ounces; these doses were given up to three times a day.—*Twenty* Phthisical patients, representing *all stages* of the disease, were treated through periods of 28 to 85 days. *Thirteen* of these cases manifested decided improvement; *four* remained stationary; and only *three* grew worse.

The detailed observations made on all these cases seem to show that the HYDRO-CINNAMIC ACID acted *not so much on the Tubercular process* itself as on the PURULENT PROCESS. *No increase of Expectoration and of Cough* took place in any case; while the benefited cases exhibited a decided increase of Appetite, of Weight, and of General Tone.

Camphor, mono-Bromated, (*Mono-brom-Camphor*),—$C_{10}H_{15}Br O$,—appears in colorless prisms, which are permanent to air and light, and have an odor both of Camphor and of Turpentine-oil.—Melting-point near 77° C [about 170 F]; boiling-point near 274° C [525 F]. Insoluble in Water; little soluble in Glycerin; *easily* so in Alcohol, fatty and ethereal Oils, Ether, Carbon Di-sulphide, and Chloroform.

JOHN STEVENSON (*Medical Press and Circular*, 1888; Oct. 24) reports that he has, since 1871, used MONOBROMATED CAMPHOR as a **Sedative** in numerous cases of **Excessive Reflex Excitability;** especially so in *Epilepsy*, *Hysteria*, *Chorea*, *Enuresis nocturna;*—and also in *Spermatorrhea* attended by chronic *Prostatitis*.

This remedy is best exhibited in doses of 0.6 gramme [9 grains], *in combination with* BELLADONNA,—this combination acting more certainly and efficaciously than either of these substances by itself.—For initial treatment, it might be well, however, to begin with doses of 0.2–0.3 gramme [3–4½ grains], and *gradually rise* to the dose stated further above.

Cannabine Tannate Merck.—J. PRIOR (*Münchener Medizinische Wochenschrift*, 1888; Aug. 14) has completed a series of comparative CLINICAL TESTS of a number of the **Cannabis Preparations** extant in the Drug-markets. His conclusive result is, that, *of all the preparations tested*, the preparation well known to both the Drug-trade and Medical literature as "**Cannabine Tannate Merck**" *produced the best effect.*—Most excellent effects were obtained by means of *this* preparation *in Forty per cent.* of the cases treated,—especially so in **Hysteric** cases and in those involving **Light Nervous Excitement.**

The Sleep caused by a properly constituted CANNABINE TANNATE *is a refreshing one, devoid* of any unpleasant accessory effects; and—what is very remarkable—*doses as small as 0.06 gramme* [*1 grain*] *were sufficient* to bring-about this beneficent effect, in cases where 0.02 gramme [⅓ grain] of MORPHINE had been employed without result!—J. PRIOR concurs with VOGELGESANG and MENDEL,—confirming the experiences of both, that Hysteric patients, who were not benefited by either MORPHINE or CHLORAL HYDRATE, *experienced happiest results from* CANNABINE TANNATE,—so that the latter drug must be declared a very desideratum for such patients.

—The "**Cannabine Tannate Merck**" is an amorphous, yellowish or brownish powder, of very faint Cannabis odor and slightly bitter, but strongly astringent, taste. It is but little soluble in Water, Alcohol, or Ether; more so in *Acidulated Water* (by a small percentage of, say, HYDROCHLORIC ACID), and quite readily so in *Acidulated Alcohol.*—As a **Hypnotic,** it is usually administered in *doses* of 0.25–0.5 gramme [4–8 grains]. An eligible formula herefor is the following:

CANNABINE TANNATE 1 gramme [15 grains]; Sugar 2 grammes [30 grains];—make 4 powders.—*One powder at bed-time.*

Colchicine for Ophthalmology.—Darier (*Par. Soc. d'Ophthalmolog.*, 1889) has published some new points on the use of the well-known Alkaloid Colchicine.

—He has witnessed excellent successes with it in *Marginal Ulcerations* of the Cornea, when of *Gouty* origin; in certain cases of *Iritis*, especially in grave forms of *Serous Iritis*, *which refuse* to yield to Salicylic preparations; in *Scleritis;* and in *Sclero-choroiditis anterior.*—These experiences of Darier's were confirmed by Abadie.

Darier ordains *Pills*, containing 0.001 gramme [$^1/_{65}$ grain] of Colchicine each, and has these administered to the *daily* number of 1–2–4, maximum 6. This dosing is, however, *to be reduced* (not wholly interrupted!) *whenever* Colic or Gastric Spasms occur. The treatment itself must be continued *in unbroken sequence until* a complete cure is effected; as interruptions may readily occasion serious relapses!

Cresol Salicylates, (*Cresylic Esters of Salicylic Acid; Salicylo-cresylic Ethers*),—**ortho-, meta-,** and **para-**;—$C_6H_4 \begin{cases} OH \\ COO(C_6H_4.CH_3) \end{cases}$.—Considering all those *Hydroxyl-derivatives of Hydrocarbons of the Aromatic Series*, in which the substitution of the "OH" for "H" has taken place in the Benzene nucleus, as Phenols,—those of them into which *but a single* "OH"-group has thus entered may be distinguished as Mono-hydroxylic (or, less accurately: "Monohydric") Phenols. Of these latter, there are known several *consecutively homologous* groups (differing by successive increments of "CH_2"):

The *Six*-carbon or *Benzene* Phenol [Carbolic Acid]=$C_6H_5.OH$;

The three *Seven*-carbon or *Toluene* Phenols [Cresols]=$C_6H_4(CH_3).OH$;

Various *Eight*-carbon Phenols [Ethyl-Phenols (including Phlorol), and Xylenols] = $C_6H_4(C_2H_5).OH$, *or* $C_6H_3(CH_3)_2.OH$; — Etc., etc., — up to *homologues as high* as $C_{24}H_{42}O$, — (the known isomers of the *Nine-* and *Ten*-carbon Phenols especially being very numerous; including the Naphthols, the Cumenols, Mesitol, Thymol, Carvacrol, Carvol, and many other well-known bodies).

—All these substances, and many of their derivatives, are more or less related in their chemical reaction on animal life: they are all endowed with some Antiseptic, Antizymotic, Bactericidal, or Antipyretic powers.—Prominent among those practically applied for

such uses in Medicine and Surgery, are especially the initial member of the series, CARBOLIC ACID,—and THYMOL. (Among the *Di-hydroxylic Phenols* and their derivatives, there are also several very important remedial substances, more or less assimilated to the foregoing in their uses;—such as, RESORCIN, GUAIACOL, HYDRO-QUINONE, EUGENOL, SAFROL, etc.)

The **Cresols,** forming the second group of the above-considered "*Monohydric*" series, are among the prominent constituents both of *Coal- and Wood-tars* (their ORTHO- and PARA-modifications principally being present).

—The peculiar physiological properties of certain **Organic-acid Esters** (or compound Ethers), formed from various PHENOLS, have attracted much attention in the last few years. Especial success as remedial agents has attended two of these combinations,—the SALICYLATES of COMMON PHENOL (of Carbolic Acid), and of BETA-NAPHTHOL,—[both better known, however, by their empiric names of "SALOL" and "BETOL"].—(Their peculiar eligibility for **Internal Antisepsis** is supposed to be dependent on their being **inert in the Stomach, but active in the Intestines;** the combination passing the ACID GASTRIC FLUID without reaction, but *undergoing dissociation into* SALICYLIC ACID *and a* PHENOL, *and consequently developing their Antiseptic action*, as soon as they reach, and react upon, the ALKALINE INTESTINAL FLUIDS.)

[Compare, hereanent, the article on "BETOL" in the BULLETIN for Oct., 1888.]

—NENCKY, the originator of both *Salol* and *Betol*, has recently prepared compounds, analogous to these, from the three CRESOLS; to wit,—**ortho-Cresol Salicylate, meta-Cresol Salicylate,** and **para-Cresol Salicylate,** (as reported to the ACADEMY OF SCIENCES at Paris; Feb. 4, 1889).

They are all crystalline, *insoluble in Water*, difficultly soluble in Alcohol, and endowed with an agreeable odor, similar to that of Salol. The *Ortho*-compound melts at 35° C [95 F]; the *Meta*- at 74° C [165.2 F]; the *Para*- at 39° C [102.2 F].

The *Ortho*-compound produces a slight burning sensation on the tongue; while the *Para*- is wholly insipid.

—*The dissociation of these three substances in the animal economy*, as above alluded-to, takes place *not only and wholly* through the action of the PANCREATIC FLUID, but is in part delayed, and accomplished through other organs, when these substances have already entered the circulation; as, for instance, in the MUSCLES! (according to the above-quoted report).—Their **Antiseptic action** is the same as that of SALOL; and NENCKY considers them still more eligible than SALOL in cases where the **Intestinal Tract** is to be treated by an agent *at once Antiseptic and Innocuous.*

—(Of course, it must be evident that the **General Toxic properties** pertaining both to SALICYLIC ACID and the CRESOLS are not removed in the combinations above described; for, from these properties, in fact, their medicinal action is inseparable;—but that simply *the most direct and immediate* portion or manner of their Toxic action, *as exercised through the Stomach when they are given separately*, is avoided by their "Esterification,"—that is, by their combination into the form of CRESOL SALICYLATES.—*Ed.*)

Mercur-beta-Naphthol Acetate, Merck.—This latest Mercury-compound has been recommended by BOMBELON (No. 98 of the *Pharmazeutische Zeitung*) as an excellent **Succedaneum for Corrosive Sublimate and for Iodoform** in *Wound-dressings.*

MERCUR-BETA-NAPHTHOL ACETATE, as prepared by MERCK, is an amorphous, rather heavy, white powder, insoluble in the usual menstrua. It is exhibited in a 1–2-% mixture with NATURAL QUARTZ POWDER (*Kieselguhr* or Silex Guhr); or by means of GAUZE; or in trituration with fresh ALBUMEN, which mixture is then shaken-up with WATER into an emulsive fluid.

BOMBELON further extols the eminently beneficent, "even life-preserving," efficacy of MERCUR-BETA-NAPHTHOL ACETATE by *Internal medication* in **Syphilitic** affections and in **Abdominal Typhus,**—being administered in doses of 0.05 gramme [¾ grain] several times per day.

Morrhuol is a brownish-yellow, oily liquid, *containing the* **Therapeutic Principles of Cod-Liver Oil.**—At ordinary temperatures, a part of the liquid crystallizes-out.—The taste of MORRHUOL is bitterish-

acrid; its odor is assimilated to that of Cod-Liver Oil;—hence it is *administered in Gelatin capsules*, containing about 0.2 gramme [3 grains] of MORRHUOL each,—which quantity *answers to about 5 grammes* [1½ *fluidrams*] *of* COD-LIVER OIL.

Recently, a CLINICAL STUDY of MORRHUOL, by Dr. EDUARD LACHASY, appeared at Paris (1888), in which the therapeutic properties of this new remedy are discussed with exceeding minuteness.

CHAPOTEAUT, some time ago, made a close research into COD-LIVER OIL and its mode of action. He prepared MORRHUOL from it, and *used this preparation successfully in desperate cases of* **Tuberculosis, Scrofula, Rachitis, etc., etc.**

—Following that, there was a study of COD-LIVER OIL by GAUTIER and MORGUES (*Journal Pharm. et Chim.*, 1888; Dec. 12), who *found several Alkaloids* in it,—notably among them: **Morrhuine.** Of the latter substance, a tablespoonful of COD-LIVER OIL contains about 2 milligrammes [1/32 grain].

The Alkaloid MORRHUINE has a special **Appetizing** effect; with **Diaphoretic** and **Diuretic** accessory effects.

The peculiar and inimitable *therapeutic effects of* COD-LIVER OIL appear to be *dependent on the presence of those Alkaloids;* which, in MORRHUOL, exist in *a higher degree* of concentration, and, consequently, also exercise their specific action with *proportionately greater intensity.*

—LAFAGE and GERMAIN-SÉE have extensively and minutely scrutinized the action of MORRHUOL in the Paris hospitals. They found it to *produce marked improvement* in **Pulmonary Catarrhs,** *Tuberculosis*, and *Scrofula;* and to *induce Mental ease*, *Food-appetite*, *and calm Sleep*,—besides a *Diminution of Expectoration.* The patients' forces "*rapidly*" *recuperated* under the influence of the MORRHUOL treatment, and the progressive *Tissue-waste was arrested.*

—In view of the fact that the COD-LIVER OIL ITSELF, in regular use, induces *Atony of the Digestive organs* and *Hypertrophy of the Gastric and Intestinal Mucous membranes*,—it will be evident that the easily digestible and well-borne MORRHUOL, representing, as it does, a TRUE EXTRACT of COD-LIVER OIL, is **the most eligible Succedaneum** for this Oil.

Narceine Meconate; *and the so-called* "Meco-narceine."—[*Additional to* "MECO-NARCEINE," *in* BULLETIN *for December, 1888:*]—Since writing the article on "MECO-NARCEINE" in last year's BULLETIN, I obtained, in original packages, the *French* preparation therein discussed.—It comes in sealed glass tubes, labeled "Solution stérilisée et titrée d'alcaloïdes méco-narcéïques"; which, on being opened, emit a strong smell of Camphor, that has evidently been added for aseptic purposes.—The content of the tubes is a yellow liquid of neutral reaction. Of the therapeutically important OPIUM-ALKALOIDS, there were found in this liquid with certainty: CODEINE, representing one-third to one-half of the total alkaloidal strength of the liquid (which strength is but 0.005 gramme to 1 cubic centimetre [equal to 2¼ grains per fluidounce]); and NARCEINE, which is, however, present in smaller quantity than the Codeine. The Bases present are bound to an Acid soluble in Ether, for whose determination the sample available did not suffice.—MECONIC ACID *was not found* in the liquid.

More recently, a preparation has been placed on the Drug-markets by another house, under the alternating names of "MECO-NARCEINE" and "NARCEINE MECONATE."—This preparation comes as a white powder, whose close examination reveals it to be a *mechanical mixture of* MECONIC ACID AND NARCEINE. Its melting-point is in the neighborhood of 110° C [230 F]. When an attempt is made to *dissolve* the mixture, *chemical union* takes place; the recrystallized product then melts at 126° C [258.8 F],—at the same time undergoing gaseous decomposition.

—**True Meconate of Narceine** has not yet, as far as I know, been described; numerous inquiries relating to it caused me to prepare it. Following is a sketch of its properties:

NARCEINE being a *Mon-acid* Base, and MECONIC ACID a *Di-basic* Acid,—the inference regarding a *Neutral Meconate of Narceine* would be, that it must contain *two* molecules of Narceine and *one* of Meconic Acid. When the attempt is made to form such a compound in this proportion, the solution containing the calculated constituents is found to crystallize *at first into yellow needles*, and *afterwards into white scales* which gather into globular aggregations. The yellow needles

are found to be *richer in Meconic Acid* than the white scales. Hence, the product is not homogeneous, and not what might have been expected theoretically.—But **a perfectly homogeneous product** is obtained by combining *one molecule each* of MECONIC ACID and NARCEINE. The **Narceine Meconate** thus constituted is of a lemon-yellow color, fairly soluble in boiling Water; poorly so in strong Alcohol; *most readily* in 50-% Alcohol. It melts, while undergoing decomposition, at the same temperature (126° C) as the salt obtained from the above-described mixture,—with which salt it appears to be identical.

Of course, the *reaction* of TRUE NARCEINE MONO-MECONATE is an *acid* one, like that of all Narceine salts, including the constitutionally neutral (or normal) ones.—I have put it on the market by the name of NARCEINE MECONATE MERCK.

Santonin; - Santoninic Acid; - Sodium Santoninate: - their Visual effects.—The phenomena of what has been regarded as a partial *Color-blindness*, which are, among other visual phenomena, superinduced by the internal use of SODIUM SANTONINATE, have been critically investigated and reviewed by Dr. H. KÖNIG (*Nature*, 1889; p. 408). It is a well-known fact that, under the influence of the *Santonin* toxication, all objects in the scope of vision *appear as seen through a yellow medium.*—Dr. KÖNIG finds the following phenomenon forming the substratum of the one just stated:—The visual power of recognizing the ulterior portion of the BLUE, and the entire extent of the VIOLET, in the Solar Spectrum, *is entirely abolished* for the time being; while the *Point of Neutrality* is situated at the wave-length of "573,"—being the exact complementary point of the suppressed VIOLET.

Dr. K. infers herefrom, that the visual phenomena occasioned by the ingestion of SODIUM SANTONINATE *do not constitute actual Violet-blindness* (consisting in an affection of the Retina or Optic nerve); but, that the rays of VIOLET light are, during the SANTONINIC toxical condition, *simply absorbed by certain of the Media of the Eye*, which have been abnormally, and, of course, only temporarily, affected in that direction by the Drug.

STRAY ITEMS.

No. 2.

IODOLE.

IODOLE *versus* **IODOFORM**, for **Ophthalmology.**

Dr. TALENTI concludes that:

1. **IODOLE** applied directly to the eye is not an irritant.

2. Its use is indicated in *Solution of Continuity of the Cornea.* Introduced into the Anterior Chamber, it exerts no injurious action on the Iris.

3. Its application is of great service in *Catarrhal Conjunctivitis* and in *Hypopyon* of *Keratitis.*

4. **IODOLE** in the form of Powder is **more efficacious** than the Ointment.

5. The different results obtained by different authors are due to the various modes of application.

6. Being Non-irritant, Inodorous, and **not more expensive than IODOFORM,** and possessing **all the antiseptic qualities** of the latter, it should replace it.

From purely esthetical considerations, not to speak of scientific value, the use of **Iodole in preference to Iodoform** commends itself to every practitioner.

—(*Medical News.*)

beneficent action exercised by IODOLE on **Suppurating Ulcerous Surfaces** has induced several Clinical investigators to adopt it for their RHINO-LARYNGOLOGICAL PRACTICE in the form of INSUFFLATIONS, *in place of the ill-odorous* IODOFORM.

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The same investigator also employs IODOLE INSUFFLATIONS in **Pharyngitis** complicated with *Follicular disease;* and has obtained very good results by IODOLE-DUSTING the *Ulcerations* on the inside surface of the cheeks.

— — *Notwithstanding* these favorable *Clinical* experiences, the process of IODOLE INSUFFLATION for the above-named purposes has, thus far, *made but slight headway in general practice*, because hitherto *the difficulty of finely and evenly distributing it over the affected surfaces* was greater than it is with IODOFORM,—owing to the lack of a proper, "non-baking," and yet finely granulated or crystallized form of IODOLE.—[Dr. SATTLER, in *Prager Medizinische Wochenschrift*, 1887; Nos. 21 and 26.]

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—Hence, in future, *there will be no longer any necessity* (as proposed by Scheffer, of Bremen, with reference to a report by Prior in *Münchener Med. Wochenschrift*, 1887; No. 38) *of resorting to a Mixture of difficultly atomizable* Iodole Powders *with a percentage of* Boric Acid, in order to facilitate their application!

—[I expect to be, within a short time, in a position to communicate reports on the experiments now being conducted, at my instance, *by several eminent Medical authorities*, relative to the application of this New Form of Iodole.]

Thalline and Thallium.—These two substances (*which have not a trace of similarity in their NATURES*) are, in consequence of *the similarity of their NAMES*, very frequently confounded by both Druggists and Physicians;—"**Thallium** Sulphate," especially, being *erroneously* ordered or prescribed in many cases where "**Thalline** Sulphate" is meant. (In the pharmaceutical *Latin* nomenclature used in several European Continental countries,—where "Thalline" is called "Thalli*num*" instead of "Thalli*na*," the similarity is, unfortunately, still more apparent.)

Numerous inquiries and communications addressed to me from professional circles show, indeed, that the confusion referred-to is wide-spread, and has taken such firm root that many medical men to-day actually believe both these names, "*Thalline*" and "*Thallium*," to signify but one substance; whereas, in truth, they signify *two substances about as different as they can be*,—**THALLINE** being **a highly complex Organic Compound,** *an artificially grouped combination of Coal-tar derivatives*,—while **THALLIUM** is **a Mineral and Elementary Substance**—*a Metal!*

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Acid, Anisic, (*Methylic Ether of para-Oxy-benzoic Acid*),—C_6H_4-(O. CH_3). COOH, — crystallizes in colorless, monoclinic prisms; melts at 180° C [356 F]; sublimes, without decomposing, at or about 280° C [536 F]. Very little soluble in cold Water; quite readily so in Alcohol.—It is a monobasic acid.

Antonio Curci (*Rivista di Terapia e Igiene*, from *Deutsche Mediz. Zeitung*, 1889; No. 12) has made numerous physiologic experiments on animals with this Acid; on the strength of which he recommends its use as follows:

1. As an **Antiseptic,** and in the treatment of **Wounds** and **Lacerations:** he finds it acting *equally to* Salicylic Acid.

2. As an **Antipyretic:** *except in Articular Rheumatism*, it is expected to act *more intensively and harmlessly than* Salicylic Acid; for Anisic Acid reduces temperature *without depressing the Heart-action*, *sustains* the augmented Blood-pressure, *does not impair* Nutrition, and induces *no Gastric disturbance.*

—For this **Internal use,** indications point to the **Sodium Anisate** as an eligible form for conveying the action of Anisic Acid.—Sodium Anisate is crystallizable, and *readily soluble in cold Water.* One of its recommendations is, that it *may safely be given in larger doses*, and is *more easily taken*, than Sodium Salicylate.

Imperialine—stated to be $C_{35}H_{60}NO_4$—is an *Alkaloid* recently discovered by K. Fragner in *Fritillaria imperialis.* It is most easily soluble in *hot* Alcohol; crystallizes in colorless, short needles; melts at 254° C [489.2 F].

As far as the researches hitherto instituted show, it is a **Heart-poison.**

—There is reason to suppose its being closely related, in its chemical nature, to the older Alkaloid **Tulipine,** discovered by Gerard in *Tulipa Gesneriana*, which plant is botanically related to *Fritillaria imperialis.* (Tulipine likewise acts as a *Heart-poison.*)

Iodole, "atomizable" (*finest crystalline Powder*), **for Insufflations for Rhino-Laryngology, etc.**—[*Additional to the general description of* "Iodole," *in* Bulletin *for June, 1888:*]—The phenomenally

beneficent action exercised by IODOLE on **Suppurating Ulcerous Surfaces** has induced several Clinical investigators to adopt it for their RHINO-LARYNGOLOGICAL PRACTICE in the form of INSUFFLATIONS, *in place of the ill-odorous* IODOFORM.

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—*But this is not all!*—Confusion, more dangerous as to its results than the above, has taken hold of the minds of some persons *who have indeed become informed as to the* **Chemical Difference** *just noted*, but

have somehow been led to consider these two substances (THALLINE and THALLIUM) *as having "identical Therapeutic Properties"!* — **This second error,**—the offspring of the one above exposed,—is still held (as my correspondence daily shows) by a number of Pharmacists and others, who have been disabused of the former misapprehension, but have *substituted* this one in its stead.

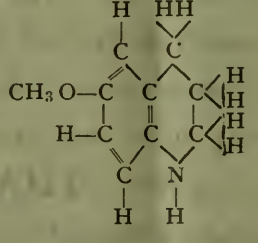
(Such error has even been induced or supported by the editorial inadvertence of PROFESSIONAL JOURNALS of high standing, as the following instance proves:

The researches made by KREIS on the **Therapeutic properties of THALLINE** were correctly reproduced in the *Medical Record*, of London; but were thence copied into *Nouveaux Remèdes* [1888; p. 42] under the mischievously misleading title of: "EFFETS DES SELS DE THALLIUM SUR LES GONOCOCCUS.")

—As a safeguard against *both* the **dangerous errors** above discussed, I shall now briefly state

THE PHYSICALLY, CHEMICALLY AND THERAPEUTICALLY DISTINCTIVE CHARACTERISTICS OF THALLINE AND OF THALLIUM.

———**"Thalline"** (called "*Thallina*" in the Latin pharmaceutical terminology of the United States and Great Britain; "*Thallinum*" in that of some Continental European countries; and "*Thallin*" in German) has the *proper CHEMICAL NAME:* **TETRA-HYDRO-PARA-QUIN-ANISOL** (or: *Tetra-hydro-para-Chin-anisol*), —being the METHYLIC DERIVATIVE of TETRA-HYDRO-PARA-OXY-QUINOLINE; = $C_9 H_{10} N (O.CH_3)$; and is supposed to have the constitution represented in the following graphic formula:



—its *CHEMICAL GENESIS* being represented by the successive stages of: QUINOLINE (Chinoline); PARA-OXY-QUINOLINE; PARA-OXY-METHYL-QUINOLINE (= *para-Quin-anisol*); TETRA-HYDRO-PARA-OXY-METHYL-QUINOLINE (= *Tetra-hydro-para-Quin-anisol*).

—PURE THALLINE appears as an *oily fluid*, forming yellowish crystals at a low temperature. It has an agreeable, aromatic odor. It is

distinctly *basic*,—forming well-defined SALTS with various Acids.—It is *not employed in Medicine in its basic state;* but, **of its Salts,** the SULPHATE has been largely thus used; likewise, the TARTRATE;—quite recently, the TANNATE and the SALICYLATE of THALLINE have also competed for place in the Materia medica.

—*The name of THALLINE*, which is suggestive of a "bright green color" (from $\delta\alpha\lambda\lambda\acute{o}\sigma$ = a shoot), has reference to the *Emerald reaction of* THALLINE SALTS *with Oxydizing agents.*—(With Ferric Chloride, for instance, this color is still produced in a solution of 1 : 100,000.)

—**THALLINE Sulphate**—$(C_{10}H_{13}NO)_2 . H_2SO_4$—is a yellowish-white, crystalline powder, having a Cumarin-like odor and an acid-saline, and also bitterish-aromatic, taste. It melts when heated above 100° C [212 F]; dissolves in 7 parts of cold or 0.5 of boiling Water, and in about 100 of Alcohol; poorly so in Chloroform or Ether.—It contains 76.9% of the Base to 24.1 of the Acid.

—**THALLINE Tartrate**—$C_{10}H_{13}NO . C_4H_6O_6$—is similar, in appearance, to the SULPHATE; its odor is suggestive of both Cumarin and Anise-oil; it is altogether less soluble than the SULPHATE,—requiring 10 parts of cold Water, several hundred of Alcohol, and being nearly insoluble in Chloroform and in Ether.—It contains 52.2% of the Base to 47.8 of the Acid.

— The **Therapeutic Value and Uses of the THALLINE SALTS** (notably the SULPHATE and the TARTRATE,—the others not having been fully tested, as yet, in this regard) are well and generally known, although it is but in 1885 that SKRAUP discovered *Thalline*, and but since 1886 that its *Salts*, piloted by v. JAKSCH, began to gain ground in the Materia medica.

Their medical properties are those of **Antipyretics, Antiseptics,** and **Antizymotics.** They are exhibited INTERNALLY, *in the first-named character*, in most various *Febrile* affections, in doses of ⅛ to ½ gramme [2–8 grains],—mostly in AQUEOUS solution, or in WINE; their taste may be corrected by ORANGE-PEEL SYRUP.—*Untoward accessory symptoms*, such as Vomit, Cyanose, Collapse, are said to be avoided by confining the doses to a low limit; large doses are to be given with precaution.

When, however, these Salts are called-upon to exhibit *not only their Antipyretic action*, but ALL THREE of the characters above named,—as in **Abdominal Typhus,** for instance, the dose-limits are usually placed at ¼ to ¾ gramme [4–12 grains].

Where a PILL is held to be preferable to a DRAUGHT, the following is an eligible formula:

> THALLINE SULPHATE (or TARTRATE) 2–6 grammes [30–90 grains]; Sugar 0.5 gramme [8 grains]; Gum Acacia 1.5 gramme [22 grains].—*Make 30 pills* (each will contain 0.06–0.2 gramme [1–3 grains] of the SALT).

The Urine takes a yellowish- to dark-brown hue, with a greenish cast, on the use of THALLINE compounds. The drug is eliminated by urination, partly unchanged, partly decomposed.

As to the claim of THALLINE *to replace* QUININE, the practitioner should bear in mind that, *although the former reduces temperature*, it has been declared to possess *no really* ANTITYPIC *action.*

— Since the appearance of *THALLINE* in the domain of INTERNAL MEDICATION, there has been considerable controversy on its alleged merits and demerits **as a Simple Antipyretic.**

The most important recent CLINICAL REPORT on the subject is that of Prof. VON JAKSCH (who originally introduced THALLINE to the notice of the Medical profession).—In *Wiener Medizinische Presse* (1888; Nos. 1 and 2) he says, under the head: "THE MODERN ANTIPYRETICS AND THEIR EFFECTS," that he has cause *to fully uphold* his formerly-enounced favorable views on THALLINE. He asserts that, in doses of 0.2–0.5 gramme [3–8 grains], it is *a perfectly certain, safe, and eligible Antipyretic*, whose effects are NOT accompanied or followed by any unpleasant accessories. He declares it to possess *the same promptness* of action as KAIRINE, *without* its drawbacks.

Nevertheless, v. JAKSCH himself *pronounces against* LONG-CONTINUED ADMINISTRATION *of even small doses of* THALLINE; which, *in the course of time*, "may be productive of dangerous, and even life-imperilling symptoms."—*On the other hand*, he considers THALLINE *the most desirable* medicine in those more rarely occurring febrile conditions which are marked by decided **Hyperpyrexia!**

— The EXTERNAL exhibition of THALLINE SALTS, *as Antiseptics*, especially in **Gonorrhea,** has attracted far more attention of late.

The researches of KREIS (*Correspondenzblatt für Schweiz. Aerzte*, 1887; No. 1) have, by "Culture" experiments, demonstrated *the extraordinary destructive effect exercised by even quite weak solutions of* THALLINE SALTS, *on the* GONOCOCCUS NEISSER, the inciter of the Gonorrheic Mucous-membrane affections. He also injected 1½–2-% AQUEOUS solutions of THALLINE SULPHATE in **Gleet,** *with extraordinary good effect.*

Dr. NACHTIGALL (*Therapeutische Monatshefte*, 1888; p. 70) advises the replacement of the THALLINE URETHRAL INJECTIONS by the use of the *THALLINE ANTROPHOR.* The ANTROPHOR is a *Medicine-bearer;* it consists of an exceedingly fine nickel-plated wire spiral, carrying within and between its coils the prepared Medicament, which has been made-up with excipients into a soft paste; so that the whole (*i. e.*,—the paste-charged spiral wire) forms a gently flexible, rather elastic, very easily applicable Succedaneum for the BOUGIE. The excipient portion of the paste consists of a GLYCERIN-GELATIN mixture, graded at such ratio that it will remain solid at medium temperature, but will liquefy in blood-warmth; it is made to contain 2–5% of THALLINE SULPHATE.—According to Dr. NACHTIGALL, the cure is thus effected—*with but two applications per day—in about half the time* (being a fortnight) which was required with the ordinary, old-fashioned Bougies.

———**"Thallium"**—in contradistinction to the substance above discussed—is the *METAL* corresponding to the elementary symbol "Tl^{III}"—having no other name or synonym or termination in any language.—(Its name is likewise drawn from the same allusion, above mentioned, to a "bright green color"; only, in this instance, the color is *not*, as in the previously described one, brought-out by chemical reactions, *but* is shown in the SPECTRUM of a flame containing this metal for its sole luminous element,—*the entire Spectrum* in that case consisting of a single, sharp and brilliant *green line.*)

THALLIUM is obtained principally as a side-product from Copper and Iron ores,—for instance, from various Pyrites, as a residuary substance in the Sulphuric-acid manufacture. In its metallic state, it much resembles Lead. It melts at 294° C [561.2 F].

—The *SALTS of THALLIUM*, especially the soluble ones, are **highly poisonous,**—producing symptoms similar to those of toxication

by LEAD, MERCURY, and others of the heavy metals.—Among those symptoms, MARMÉ [*Nachrichten der Königl. Akad. der Wissensch.*, Göttingen, 1867; No. 20, Aug. 14] found irregularity and arrest of the *Heart-action.* Taken into the stomach, even in minute quantity, they induce *Gastro-enteritis*, accompanied by violent, even bloody *Diarrhea;* added thereto, there are *Pulse-ataxy*, *Trepidation*, *Motor-paralysis*,—appearing to be of Central origin. Dogs are killed by internal doses of 0.5–1.0 gramme [8–15 grains]. With subcutaneous administration, the lethal dose is much smaller.—PAULET LAMY and GRANDEAU agree with MARMÉ as to the *Topically Toxic* character of the THALLIUM SALTS.

As far as is shown by the very voluminous literature at my command, a **Therapeutic Use of Thallium Salts** *has been attempted but once.* It was done by POZZI and COURTADE ("Note sur le Traitement de la Syphilis par le Thallium,"—*Gazette Médicale de Paris*, 1884; No. 13, Mar. 29). They employed **THALLIUM Iodide**, in doses of 1 centigramme [1/6 grain], by Pill, in *Erosive* and in *Hypertrophic Secondary Syphilides* on the Vulva. Their inferences from these experiments are as follows:

> "1. THALLIUM IODIDE is an **Alterative.**
>
> "2. It is of curative influence in **Syphilis.**
>
> "3. It passes into the circulation, and is recoverable from the *Urine.*
>
> "4. Its efficacy is *inferior* to that of MERCURY.
>
> "5. Its use induces somewhat alarming accessories: *Gastric spasms*, *Vomition*, *Stomatitis.*"

— — —In view of what has been here adduced, the **Great Danger of confounding THALLINE and THALLIUM,** *especially* when using the latter instead of the former IN INTERNAL MEDICATION, must become evident to every reader.

— **On the other hand,** *the question is still open*, whether THALLIUM SALTS (f. i., the Sulphate) *can be used similarly to those of* THALLINE, with good effect, for *Injections in Gonorrhea* (as some of the private communications addressed to me, and previously referred-to, state it to have been used) and in other EXTERNAL USES of similar nature.

> [☞ ***Communications*** *on well-recorded observations in this latter direction, from Professional Gentlemen, will be very acceptable to the Editor of* MERCK'S BULLETIN.]

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IN EITHER MEDICINE OR TECHNOLOGY.

. . . . .

WITH AVERAGE VALUES AND SYNONYMS AFFIXED.

A GUIDE

For the Physician, Apothecary, Chemist and Dealer.

BY

E. MERCK.

1889.

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CONTENTS.

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MAXIMAL DOSES OF NEW REMEDIES.

Numerous inquiries addressed to me by Physicians and Pharmacists in regard to the DOSAGE OF NEW REMEDIES have prompted me to compile, as below given, the **Maximal Doses** of those Medicaments, as far as they are known to have been therapeutically demonstrated.

For the material of this compilation, I am indebted principally to B. FISCHER'S *Neuere Arzneimittel;* Berlin, 1889; and to Prof. AUREP'S and Dr. VOROMIKIN'S *Russian Medicinal Agenda*, 1889, I.—The authority of these scientists in the domain of Pharmacology being unquestioned, I trust the statements given may be received with confidence.

MEDICAMENT.	Maximal Adult Dose, *by Mouth.*			
	SINGLE.		DAILY.	
	Grammes	= about Grains	Grammes	= about Grains
Acid, Cubebic	1	15	5	75
" Hydrobromic, diluted (10%)	*forty Drops*		*one hundred Drops*	
" Iodic	0.3	4½	1.2	18
" Per-osmic	0.015	¼	0.05	¾
" Sclerotic	0.06	1	0.25	4
" Valerianic	*ten Drops*		*forty Drops*	
Adonidin	0.006	1/10	0.03	½
Agaricin	0.015	¼	0.05	¾
Allyl Tri-bromide	*eight Drops*		——	——
Aloin	0.3	4½	0.6	9
Amylene Hydrate	4	60	8	120
Anemonin	0.03	½	0.1	1½
Antifebrin	1	15	3	45
Apiol, crystallized, (*solid* Parsley-camphor)	1	15	4	60
Apo-Codeine	0.03	½	0.08	1¼
Apo-Morphine Hydrochlorate	0.01	⅙	0.05	¾
Arbutin	1	15	4	60
Arsenic Bromide	0.01	⅙	——	——
" Iodide	0.01	⅙	——	——

of CHROMIC ACID as an **Escharotic** *in the Nasal and Pharyngeal cavities*, date back as far as 1885. In that year appeared, almost simultaneously, the reports of BRESGEN[1], HERYNG[2], RETHI[3], and SCHWANEBACH[4], on the Escharotic Uses of CHROMIC ACID. These investigators fitted the ACID for these uses, either by taking-up some of it in a molten condition, on the end of a metallic probe; or by agglutinating a crystal of it to a moistened glass rod; or by fastening it in pincers;—taking care to envelop the sides of the Acid lump with cotton-wool *for isolation.*

The experimental results obtained by the investigators named may be sufficiently recapitulated here in HERYNG's words:

> "CHROMIC ACID is an *Energetic Caustic,—barely painful*, and *very slightly irritating* to Mucous membranes.—**Inflammative growths, Granulations,** soft **Polypi** and **Adenoid** formations, various **Ulcerations,** and soft, spongious **Hyperplasias,** are treated by it most successfully.—The *Escharotic effect* is attained at the expense of an extremely small consumption of the *Caustic material;* and any excess of the latter is to be neutralized after the operation by SODA SOLUTION. In **Chronic Catarrhs,** resulting in *Hypertrophia and Tumescence of the Nasal cavity*, the effect of CHROMIC-ACID topical applications surpasses that of all other hitherto employed means of treatment."

Despite these manifest and well-authenticated virtues of CHROMIC ACID as a **Topical Caustic,** many voices have at times been raised against it in just that character, on account of the difficulty sometimes experienced *in localizing its action* within the closely circumscribed affected surfaces, and the consequent danger of its *cauterizing the adjacent healthy parts.* This objection is unfortunately but too well founded, as regarding most of the *so-called* "Medicinal" brands of CHROMIC ACID to-day in the markets of the world, insofar as *hardly any* such preparations are found to be **wholly free from Sulphuric Acid.** *This is the sole point* on which the objection just mentioned hinges. For it is merely the SULPHURIC ACID with which most CHROMIC ACIDS are contaminated, that makes them *easily deli-*

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(1) BRESGEN in *Revue Mensuelle de la Laryngologie*, 1885; No. 10.

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[*This point was specially discussed in the* BULLETIN *for April, 1888;* and the TEST was there described, which may be employed for *conclusively proving the absence of* SULPHURIC ACID *from* **Merck's Chemically Pure Chromic Acid—crystals or sticks!**]

— — *The same question* (regarding the freedom of CHROMIC ACID from SULPHURIC) seems to have furnished the motive for a General Order by the ROYAL PRUSSIAN WAR DEPARTMENT, (*supplementary to the one mentioned in the* BULLETIN *for Dec., 1888*), requiring all ARMY SURGEONS to *employ none but Chemically Pure* CHROMIC ACID in the treatment of **Foot-sweat** among the troops.—In one of the cases treated as described in the previous order, inflammation and Chromium toxication had ensued; whereas, a 2–5-% AQUEOUS SOLUTION of ABSOLUTELY NON-SULPHURIC CHROMIC ACID, applied to the *unbroken cuticle* of the Sole of the human foot, as originally directed by the DEPARTMENT, *will never exercise any but a Tanning and Toughening Action* on the cuticle,—free from all untoward, caustic, or inflammative effects!

"Pyrodin"—*so-called*; OR: **"Hydracetin"**; OR, *properly:* **Acetyl-phenyl-hydrazin.**—This **Antipyretic** was chemically and therapeutically described *in last February's* BULLETIN under the *third* —the *only* chemically exact one—of its three foregoing names. Since that publication, the researches of J. GUTTMANN in Berlin (BERLINER MEDIZINISCHE GESELLSCHAFT; Session of May 1, 1889), the principal results of which are recapitulated below, have thrown additional lights on both the PHYSIOLOGICAL and the THERAPEUTIC action of this substance.

—[N. B.—The GERMAN "Pyrodin"—that is, **the chemically pure** ACETYL-PHENYL-HYDRAZIN "MERCK"—was the substance experimented-with by Dr. GUTTMANN.—Its difference from the *British* product called "Pyrodin" is pointed-out in the *February* BULLETIN, as mentioned above.—ED.]

—Doses of 0.25–0.50 gramme [4–7½ grains] *injected subcutaneously*, produced DESTRUCTIVE EFFECTS on rabbits. The autopsy showed distinctly a *disorganization of the red blood-corpuscles* in the kidneys, the liver, and the vascular system. This effect is ascribable to the strongly *Oxygen-absorbent action* of the ACETYL-PHENYL-HYDRAZIN.

Medicament.	Maximal Adult Dose, *by Mouth.*			
	Single.		Daily.	
	Grammes	= about Grains	Grammes	= about Grains
Pereirine Hydrochlorate	0.5	7½	2	30
Phen-acetin (para-Acet-phenetidin)	1	15	2	30
Picro-toxin	0.006	1/10	0.02	⅓
Piperine	0.6	9	1.2	18
Podophyllo-toxin	0.02	⅓	0.06	1
Potassium Osmate	0.015	¼	0.05	¾
Propyl-amine, *so-called,* see Tri-methyl-amine.	....	.....	....	.....
Pyridine	——	——	*twenty-five Drops*	
Quinoline (Chinoline) Tartrate	2	30	6	90
Resorcin	3	45	10	150
Salicin	2	30	10	150
Salol	2	30	10	150
Silver Cyanide	0.005	1/12	0.02	⅓
" Iodide	0.02	⅓	0.06	1
Solanine	0.1	1½	0.5	7½
Sparteine Sulphate	0.03	½	0.1	1½
Strophanthin	0.0002	1/333	0.0004	1/166
Sulphonal	4	60	8	120
Terpin Hydrate	0.3	4½	1	15
Terpinol	0.3	4½	1	15
Thalline Sulphate	0.5	7½	1.5	23
" Tartrate	0.5	7½	1.5	23
Tincture Strophanthus	1.5	23	5	75
Tri-methyl-amine (*erroneously called* "Propyl-amine")—10-per-cent. *Solution*	3	45	10	150
Urethane	5	75	——	——
Xylene (Xylol)	2	30	——	——

N. B.—*All the above-stated* **Sizes** *of Dose are calculated for administration* **by Mouth** *only.*

The original statements by Clinical Professors, from which the figures in the above Table were drawn, being mostly given in Metrical Weight (*Grammes*), I have, for the convenience of the reader, here added their *approximate equivalents* in Grains. This was done—*as nearly as the necessary regard for compact and practical forms of fractions would permit*—on the commonly adopted **Ratio of 1:15** (One Gramme as equaling Fifteen Grains).—If it should appear desirable to turn the above-given—*original*—Gramme statements into Grains *on a more accurate basis*, this may be done by multiplying each Gramme Weight with the number "**15 1/2**"; or, *still more accurately*, with "**15.432.**"—Ed.

Dosing for Children and Aged Persons.

With all **Powerful Medicaments,** the following rules (according to *Journal de la Pharmacie et de la Chimie*, 1889; p. 582) ought to be observed:

A.—For Children.

The ADULT DOSE (being for persons *between 21 and 60 years* of age) is to be supposed divided into **21** equal parts, and the CHILD'S DOSE is to consist of *as many of these parts* as there are *years in the child's age.*

$$\textit{Ratio:} \left\{ \text{Child's Dose} = \frac{\text{Adult Dose} \times \text{Child's Years}}{21} \right\}.$$

(Thus, for instance, if the proper Adult Dose of a powerfully active substance were "7 grains"; then the proper dose of the same for a Child of 4 years would be: Grains 7 *divided by 21* and multiplied by 4; or: $\frac{\text{gr. vii} \times 4}{21}$, $= \frac{\text{gr. iv}}{3}$; or: One grain and one-third.)

— **Remark.**—FOR CHILDREN, it is usually considered advisable to **reduce** the doses of *Sedatives and Hypnotics* somewhat **below** what they would have to be by the above rule; and to **increase** the doses of *Laxatives and Cathartics* somewhat **above** what they would be by the rule.

B.—For Aged Persons.

The proper ADULT DOSE (supposed to be intended for persons between the ages of 21 and 60) is usually to be *lessened for persons above 60 years*, on the following principle: —The DOSE FOR THE AGED is equal to the regular ADULT DOSE *multiplied by 60 and divided by the patient's age in years.*—*Ratio:* $\left\{ \text{Aged Dose} = \frac{\text{Adult Dose} \times 60}{\text{Patient's Years.}} \right\}$.

(Thus, for instance, if the proper Adult Dose of a powerful medicament were "40 drops"; then the proper dose of the same for an Aged Person of 80 years would be: Drops 40 *multiplied by 60* and divided by 80; or: $\frac{\text{gtt. xxxx} \times 60}{80}$, $=$ gtt. xxx; or: Thirty drops.)

Acid, Chromic,—absolutely free from Sulphuric Acid.—Its use in Rhino-Pharyngeal Affections.—[*Additional to* BULLETIN *for April and for Dec., 1888:*]—Observations, showing the eligibility

of CHROMIC ACID as an **Escharotic** *in the Nasal and Pharyngeal cavities*, date back as far as 1885. In that year appeared, almost simultaneously, the reports of BRESGEN(1), HERYNG(2), RETHI(3), and SCHWANEBACH(4), on the Escharotic Uses of CHROMIC ACID. These investigators fitted the ACID for these uses, either by taking-up some of it in a molten condition, on the end of a metallic probe; or by agglutinating a crystal of it to a moistened glass rod; or by fastening it in pincers;—taking care to envelop the sides of the Acid lump with cotton-wool *for isolation.*

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—GUTTMANN's therapeutic experiments have fully confirmed the earlier observations of DRESCHFELD, as to the **marked Antipyretic action** of this medicament in *Abdominal Typhus*, *Pulmonary Phthisis*, *Scarlatina*, *Erysipelas*, *Acute Miliary Tuberculosis*, and *Septicaemia;* for he succeeded in obtaining a considerable DEPRESSION of TEMPERATURE, *lasting 5–6 hours*,—and more in some cases,—*by the administration of but 10–15 centigrammes* [1½–2¼ grains] of ACETYL-PHENYL-HYDRAZIN.

—Used as an **Analgetic**,—the dose of 10 centigrammes [1½ grain] suffices, in *Acute Articular Rheumatism*, to procure relief, and, in some instances, complete cessation of pain. (It is to be noted, however, that this substance is, of course, **only a Palliative,** which can exercise no effect on the actual morbid process !)

In *Ischias*, a single dose of 0.05 gramme [¾ grain] would usually procure a cessation of pain for hours.

—The ACETYL-PHENYL-HYDRAZIN was also tested as an **External Germicide.**—In *Psoriasis*, 10-per-cent. OINTMENTS of it were employed with *curative effect.*

— —In relation to the above-mentioned *Internal Uses* of ACETYL-PHENYL-HYDRAZIN, the following inferential rules are drawn by GUTTMANN from his experiments and observations :

> "1.—The ACETYL-PHENYL-HYDRAZIN is used with best total effect in **Doses** *not exceeding 10 centigrammes* [1½ *grain*] **per day;** and, be it noted, when intending to produce palpable effects **in High-feverish conditions,** this "Daily Dose" should be given in the shape of a SOLE SINGLE DOSE; OR—AT MOST—in the division of *two single* doses of 5 centigrammes [¾ grain] each,—*one hour apart!*
>
> "In **Multiplex Acute Articular Rheumatism,** however, the above-stated DAILY DOSE of 10 centigrammes IS MOST ELIGIBLY GIVEN *in two Singles* of 5 centigrammes [¾ grain] each; placing one in the *forenoon* and the other in the *afternoon!*
>
> "2.—The above-stated DAILY DOSES of 10 cgm. (whether divided or whole!) should *not be administered on more than* **three successive days;** *then suspended* for an interval, and then repeated *in similar order* as necessity may appear.
>
> —"The foregoing PRINCIPLES OF DOSING, when followed, will carry a *guarantee of success* as to the ANTIPYRETIC action in HIGH FEVERS, and as to the ANALGETIC effect in ARTICULAR RHEUMATISM and NEURALGIA!"

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NEW ANTIPYRETICS (and Analgetics).

The BULLETIN for February, 1889, in discussing ACETYL-PHENYL-HYDRAZIN (also called "HYDRACETIN" and "PYRODIN"—under which latter name it has again been treated in the BULLETIN for June, 1889), showed the *close chemical relation* existing between this substance and several previously discovered medicaments which had already earned good repute for themselves. These others were ANTIFEBRIN, ANTIPYRINE, ANTITHERMIN, and PHEN-ACETIN (PARA-ACET-PHENETIDIN);—all four being more or less famous as **Antipyretics** or **Analgetics,** or both.

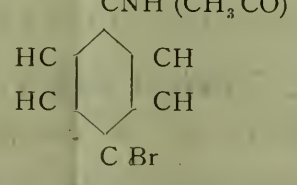
The inference drawn at the close of the February-BULLETIN article here referred-to was that,—these last-mentioned four substances *being closely inter-related* BOTH *in their Chemical Constitutions* AND *in their Therapeutic Actions*, and the new claimant for medicinal distinction appearing to belong *to this same chemical* "family group,"—it might fairly be presumed to belong *to this same therapeutic* class likewise!

This inference has since been shown to have been correct, as demonstrated by the Clinical Reports quoted in the Article on "PYRODIN" (ACETYL-PHENYL-HYDRAZIN) in the June BULLETIN.

—Now, there is again a chance group of THREE NEW, OR NEWLY APPLIED, COMPOUNDS, partaking of **the same general chemical and therapeutic characteristics** that distinguish the above-mentioned five substances; and the confidence with which clinical experimenters have at once on their appearance received these new-comers is due in no slight measure to their *evidently close chemical relation to that older and favorably known group of Antipyretics and Analgetics.*

> [For evidence as to the close chemical relation here mentioned, the reader may *compare the formulas* of the three "new-comers," as hereinafter given under the heads of "ANTISEPSIN," "EXALGIN," and "METH-ACETIN," with the formulas discussed on page 14 of this year's BULLETIN (Feb. No.), under the head of "ACETYL-PHENYL-HYDRAZIN," etc.—ED.]

"Antisepsin" (*properly:* **para-mono-Brom-phenyl-acet-amide;**—OR, *briefly, and sufficiently exact:* **"Bromated Antifebrin"**)—



—was slightly discussed in the BULLETIN for June and for August, 1888, under the title of: "BROM-PHENYL-ACET-AMIDE, Mono-."

[*The name* "ANTISEPSIN" for this substance, as indicative of *one* of its principal *uses*, is a brief substitute proposed by some clinical practitioners in place of the cumbersome *but exact* chemical designation "PARA-MONO-BROM-PHENYL-ACET-AMIDE."—The name "BROMATED ANTIFEBRIN," however, may be safely assumed, by this time, to be quite as suggestive—though it be *indirectly* so—BOTH of *all its various uses* AND of *its chemical nature;* for, the chemical constitution and the therapeutic applications of ANTIFEBRIN (*Medicinal Phenyl-acet-amide!*) being proverbially familiar to the Professions, it needs but a reminder that BROMINE is introduced by substitution for a Hydrogen-atom in ANTIFEBRIN, to give at once a complete characteristic of the compound—both chemical and therapeutic. (See BULLETIN for *June*, 1888.)—ED.]

BROMATED ANTIFEBRIN (PARA-MONO-BROM-PHENYL-ACET-AMIDE; or "ANTISEPSIN") is devoid of odor and taste; it crystallizes in small, pearly prisms, melting—according to exact recent determination—at 164.5° C [328 F]. It is *insoluble in cold Water*, difficultly soluble in hot; only slightly in Glycerin; *easily soluble*, however, in Alcohol or Ether. A *one-per-cent. Alcoholic solution* suffers the addition of twice its volume of Water, or of thrice its volume of Glycerin, without clouding.

Prof. CHIRONE (*Il Morgagni*, 1888; Oct. and Nov.), having tested the **Physiologic effects** of BROMATED ANTIFEBRIN on various animals, reports as follows:

1.—"ANTISEPSIN" (BROMATED ANTIFEBRIN) is quite well applicable **Subcutaneously**; the smaller doses occasioning *no local symptoms* whatever, and the larger ones being productive only of Hyperemia and a slight Serous infiltration, but *never* of Inflammation or Suppuration.—*By the stomach*, quite large doses are required for inducing a mentionable degree of irritation.

2.—After **Small doses,** the most prominent symptoms are: *Mydriasis*, *Reduction* of Temperature, *Cold* Tremors, *Acceleration* of the Peristaltic movement, *Augmentation* of the Urinary secretion.

3.—After **Strong, Toxical doses:** *Intensive* Mydriasis, *Shakes*, *Spasms*, *Progressive* Reduction of Temperature, most frequently accompanied by *Reduced Frequency* of the Cardiac Systole, Disturbed *Respiration*, *Hemoglobinuria*, *Glycosuria.*—Death results through Asphyxia; the Heart being, meanwhile, the last to die.

4.—The **Smallest Toxical Subcutaneous dose** was found to be: With Dogs, 45 parts per weight *to one million* of the animal's weight; with Rabbits, 20 to 40 parts; with Guinea-pigs, 40; with Chickens, 20 to 40.—**By Mouth,** the Smallest Toxical dose with Dogs was determined at 120 *one-millionths* of the animal's weight.

"Exalgin" (*properly:* **Methyl-phenyl-acet-amide;** — OR: **"Methylated Antifebrin"**)—$C_6 H_5 N\left\{\begin{matrix} CH_3 \\ C_2 H_3 O \end{matrix}\right\}$—is another of the *chemically and therapeutically inter-related* group of EIGHT ANTIPYRETICS above pointed-out, under "New Antipyretics" (page 53).

[Its formula indicates that it is a DIRECT DERIVATIVE OF ANTIFEBRIN, formed by the substitution of a *Methyl-group* for a Hydrogen-atom in the original PHENYL-ACET-AMIDE,—as demonstrated by HEPP, the investigator of ANTIFEBRIN, already in the year 1877. The short and therapeutically significant, but chemically meaningless, name "EXALGIN" (from Greek ἐξ = "*out of*," and ἄλγος = "*pain*") was given it, nearly two years later, by its French sponsor, BRIGONNET, in just recognition of its **Analgetic** properties, which bid fair to outrank even its **Antifebrile** powers.—The name "METHYLATED ANTIFEBRIN" is suggested by, and is at the same time sufficiently indicative of, its chemical constitution; and also of its principal therapeutic properties;—*on the same principle* as has been indicated for the choice of the name "*Bromated Antifebrin*" for "*para mono-Brom-phenyl-acet-amide.*" (See page 54.)—ED.]

METHYLATED ANTIFEBRIN (METHYL-PHENYL-ACET-AMIDE; or "EXALGIN")—according as it has been obtained either by melting or by crystallization—appears either in flat white tablets or in fine white needles. It melts at about 101° C [or 214 F]; is but sparely soluble in cold Water, more so in hot, most readily in a mixture of Water and Alcohol.

Its **Analgetic** powers have been highly extolled by the eminent French therapeutists: DUJARDIN-BEAUMETZ and BARDET.

Its **Physiological** action, as ascertained by experiments on animals, is exercised principally and energetically through the *Spinal cord.* The dose of 46 parts *to one hundred thousand* of the animal's

weight was found to act lethally on rabbits,—the precursory symptoms being *Muscular tremors* and *Respiratory paralysis.*

Small Doses cause the *Capacity for Pain to be suppressed* entirely, while the *Tactile Sense remains unimpaired;* meanwhile, the *Temperature slowly decreases.*

The physiologic effects of METHYLATED ANTIFEBRIN bear great general resemblance to those of ANTIPYRINE; but their restrictive force appears to be directed more toward the *Sensorial* than the *Thermogenic* (Heat-producing) centres.—

> [Hence, it has come into prominence more as an **Analgetic** than as an **Antipyretic,** so far.—ED.]

The *Analgetic Dose* of METHYLATED ANTIFEBRIN is placed at 0.25–0.40 gramme [4–6 grains] for a *Single* administration; or 0.40–0.75 gramme [6–11 grains] for *Two* administrations within 24 hours. Its Analgetic effect thus largely exceeds that of ANTIPYRINE, *especially* so in *all* **Neuralgias,**—including the *Intestinal* ones.

So far, NO *Gastric or Intestinal irritations*, NOR *Cyanose*, have been noticed to survene upon the use of METHYLATED ANTIFEBRIN as directed. The drug is *eliminated through the Urine;* it *reduces the quantity* of the urinary secretion, and—like the other Antithermic remedies of this chemical group—it *acts reductively on both the Polyuria and the Saccharine strength of Diabetic urination.*

—BARDET recommends the following formulas:

> 1.—METHYLATED ANTIFEBRIN 2.5 grammes [38 grains]; Cherry Cordial 40 grammes [600 grains];—*dissolve;* then *add:* Distilled Water 80 grammes [1200 grains]; Simple Syrup 30 grammes [450 grains].—*One to three tablespoonfuls in 24 hours.*
>
> 2.—METHYLATED ANTIFEBRIN 2.5 grammes [38 grains]; Rum 40 grammes [600 grains]; Distilled Water 110 grammes [1650 grains].—(*Dose as above*, in formula No. 1 !)

Meth-acetin (*properly:* **para-Acet-anisidin** [*Acetyl-methyl-para-Amido-phenol*];—OR: **"Oxy-methylated Antifebrin"**)—

$$C_6H_4 \begin{cases} O\,CH_3 \\ NH\,.\,C_2H_3O \end{cases}$$

—is yet another member of the above-discussed group.

[The convenient name "METH-ACETIN" for this compound is evidently formed by contraction from its *two exact chemical names*, as above given; but *in itself* it bears no precise assurance of what is meant.—The name "OXY-METHYLATED ANTIFEBRIN" will *both* show the therapeutic relation of this medicament to one of the best-known standard Antipyretics, *and* also indicate its chemical composition. For, just as its parallel, PHEN-ACETIN—or: *para-Acet-phenetidin;* or: *Acetyl-ethyl-para-Amido-phenol*—$C_6 H_4 \left\{ \begin{matrix} O\ C_2 H_5 \\ N\ H\ .\ C_2 H_3 O \end{matrix} \right.$—(briefly noticed in the BULLETIN for April, 1888, and on page 14 of February's number of the present year) was shown to differ from ANTIFEBRIN by the substitution of an *Oxy-Ethyl* group for a Hydrogen-atom, so the METH-ACETIN may be considered as ANTIFEBRIN with an OXY-METHYL group substituted for a Hydrogen-atom.—Hence, PHEN-ACETIN and METH-ACETIN might be called "OXY-ETHYLATED ANTIFEBRIN" and "OXY-METHYLATED ANTIFEBRIN," respectively,—to show, in an easily pronounceable form, their chemical relation to the most widely employed member of their group.—ED.]

The METH-ACETIN employed by F. MAHNERT in his experiments ("Ueber die antipyretische Wirkung des Methacetins": *Wiener Klinische Wochenschrift*, 1889; No. 13) is described as a crystalline powder, of slightly reddish tinge, consisting of tabular leaflets; odorless; of faintly saline-bitterish taste; melting at 127° C [260.6 F]; sparingly soluble both in hot and in cold Water, but very easily so in Alcohol.

As might have been presumed from its chemical constitution, so closely parallel to that of PHEN-ACETIN, it appears that METH-ACETIN has, in experiment and practice, developed **Physiological properties** quite similar to those of its parallel compound.

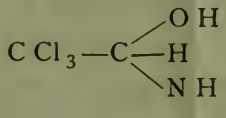
The LETHAL INTERNAL DOSE for *rabbits* was found to be about 3 grammes [45 grains]; death was preceded by a considerable *Reduction of temperature* and by a decided affection of the *Central nervous system*, evinced in *Spasms*. The URINE of the object-animals exhibited *reducing* reactions and was *free from Hemoglobin*.

The THERAPEUTIC ACTION of METH-ACETIN, *on Children*, in Doses of 0.15–0.2 gramme [2¼–3 grains], is **Antithermic.** The Reduction of temperature takes place gradually and is of variable duration. Frequently, in MAHNERT'S investigations, *heavy sweats* ensued; but no untoward accessory symptoms were noticed.

The **Antiseptic** qualities of METH-ACETIN are demonstrated by its *one-per-cent.* solution arresting the decomposition of Milk and preventing the ammoniacal fermentation of Urine.

CHLORAL-URETHANE and URALIUM.

Chloral-Urethane is the product of simple addition of one molecule each of CHLORAL (NOT *Hydrate!*) and ETHYLIC URETHANE (*Common Urethane!*). Hence, it is represented by the formula:



It is a crystalline mass, *insoluble in cold Water*, and by *boiling* Water decomposed into its two parent components. Alcohol and Ether both dissolve it readily; Water separates it again from these solutions. It melts at about 103° C [217 F]; after, however, partially decomposing from 100° C [212 F] upward.

CHLORAL-URETHANE was first systematically investigated in regard to its *Therapeutic properties*, parallelly with ETHYLIDENE-URETHANE and METHYLIC URETHANE, by HÜBNER and STICKER (*Deutsche Medizinische Wochenschrift*, 1886; No. 14, p. 236). The *last-named two* compounds were found to be *totally inert* in doses of 1–4 grammes [15–60 grains]; while the CHLORAL-URETHANE was found to produce **Hypnotic** effects, similar to those of ETHYLIC URETHANE, although *less certain* and *less persistent.* In some cases it appeared also to give **Sedative** effects; for instance, in *Ulcus ventriculi.*

MAIRET and COMBEMALE ("Note sur l'action physiologique du Chloral-uréthane": *Montpellier méd.*, 1886; p. 149) reported, about the same time, on an extended series of *Animal-experiments* with CHLORAL-URETHANE. Their principal conclusion was: that the **Toxic effect** *outweighs the Hypnotic* in prominence and importance of symptoms. The SLEEP that had been induced by the medicament was invariably *attended by a Paralysis* of the hinder parts; LARGE DOSES (from 40 parts per 100,000 of the animal's weight), in dogs, caused *Diarrhea*, profuse *Diuresis* and *Salivation*, difficult *Respiration*,

slight disturbances of *Compensation*, *Itching* of the skin and nose; BUT NO SLEEP!

Uralium, according to GUSTAVO POPPI'S report to the SOCIETÀ MEDICO-CHIRURGICA DI BOLOGNA, is a **new Hypnotic,** discovered by him. This compound is here discussed in connection with CHLORAL-URETHANE, because, according to POPPI (*Riforma Medica*, 1888; No. 81) it is *likewise a combination of* URETHANE *with* CHLORAL, and *possesses the same quantitative chemical composition as* CHLORAL-URETHANE!

URALIUM appears in crystals of bitterish taste, which are readily soluble in Alcohol,—*less so in Water*. The melting-point has not been determined as yet.

Doses of 80–90 parts per 100,000 of the animal's weight, in dogs, ALWAYS INDUCED SLEEP, commencing after 1–2 hours and lasting 5–10 hours. The animals *bear the* URALIUM *better than* CHLORAL HYDRATE, because the former medicament *does not reduce the Temperature so much*, and also produces no disturbance in the general tone.

Human experiments were instituted by POPPI first on his own person. He took 1–2 grammes [15–30 grains] of URALIUM in the evening,—experiencing, in consequence, an *increased frequency of the Pulse* (up to 75 or 80), *Somnolency*, and a sensation of *Debility*. The Sleep thus induced did not last longer than the ordinary sleep; on awaking, the experimenter felt but a slight, transitory *Lassitude*.

—Thereafter, the investigator tried the effects of URALIUM on numerous Clinical patients,—embracing cases of Alcoholism, Phthisis, Heart-disease, Insanity, and Nerve-ailments. The experiments proved that URALIUM, in doses of 2–3 grammes [30–45 grains] PRODUCES CALM, ENDURING SLEEP.—In otherwise healthy individuals, suffering only from INSOMNIA, *the blood-pressure is not affected*. This is a decided advantage possessed by URALIUM over CHLORAL HYDRATE, and which, in addition to its cheapness, well deserves consideration.

— —Although the *analytical formulas* of URALIUM and of CHLORAL-URETHANE are reported to be absolutely *identical*, and hence the view

of the identity of these preparations seems to be supported,—still, *the differing physiological results* of the investigations by POPPI and by MAIRET-COMBEMALE speak for the assumption that they are *two different compounds!*—Hence, it will be well to await further reports on URALIUM, which shall convey clear perception of its chemical constitution.

Nicotine bi-Tartrate (*Acid Tartrate*).—The manufacture of this salt having been confided to me by the inventor of the process, Dr. med. DRESER of Strassburg, Alsace, I will state the reasons which have led to its introduction.—This salt is *beautifully crystalline*, and *quite stable;* while, on the one hand, all the other known simple SALTS of Nicotine are open to the objection of very difficult crystallization, in consequence whereof the strengths of their solutions become variable and unreliable; and, on the other hand, the solutions of the *free* ALKALOID possess the tendency of resinifying, thickening and darkening, which makes them therapeutically ineligible.

NICOTINE BI-TARTRATE, when prepared according to DRESER'S formula, crystallizes in fine white tufts of needles, and is *very readily soluble* in Water. Its composition, on analysis, shows the following proportions:

$C_{10} H_{14} N_2$ [NICOTINE]:	32.53%
$2 C_4 H_6 O_6$ [TARTARIC ACID]:	60.51 "
$2 H_2 O$ [WATER]:	7.34 "

The PHYSIOLOGICAL EXPERIMENTS so far made with this preparation (*Archiv der Pharmacie*, 1889; p. 269) had Frogs for their objects. They demonstrated conclusively that the well-known specific effects of the PURE ALKALOID are all produced by this salt *likewise*, and *in like degree.* Among them were conspicuously evident: the strong stimulation of *Dermic secretion*, as shown by the Copious frothing of the surface; the effect on the *Central nervous system*, as shown by excited saltations, clonic twitchings and spasms; the stimulation of the terminal portions of the *Motor-nerves*, as shown by the resultant peculiar muscular jerks.

STRAY ITEMS.

No. 3.

DIGITALIN.

Constantly recurring inquiries, and other evidences of uncertainty existing in the minds of Professional people, regarding **the various "DIGITALINS"** of commerce, prompt me *to repeat, here,* an extract from a fully detailed comparative statement made on this subject in a CIRCULAR issued by my DARMSTADT HOUSE in August, 1886.—E. M.

Merck's German preparations [Nos. 1 & 2]:	*correspond to*	**The French preparations** [Nos. 1 & 2]:
1. **Digitalin, pure, amorphous,** *Ph. Gallic. and Ph. Belg.*		1. **Digitaline amorphe du Codex** (*Digitaline amorphe* HOMOLLE).
2. **Digitoxin, chem. pure**		2. **Digitaline crystallisée du Codex** (*Digitaline crystallisée* NATIVELLE).

3. **Digitalin Germanic Merck, pure, powder,** is a preparation of *constantly uniform composition and effect;* it consists *principally of* DIGITALEIN, with some DIGITONIN and some of the DIGITALIN OF SCHMIEDEBERG.

4. **Digitin,** *an inert body,* is by some called "CRYSTALLIZED DIGITALIN."—(*Not to be confounded,* therefore, with the similarly named French officinal preparation No. 2, above!)

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Amylene Hydrate, pure, medicinal,—Kahlbaum.—[Additional to BULLETIN for April, 1888:]

That excellent **Hypnotic,** AMYLENE HYDRATE, exhibits a peculiarity shared by several substances of this class; to wit,—that its HYPNOTIC ACTION is PURE AND INNOCUOUS, *devoid of Accessory or Subsequent Symptoms*, when THE MEDICAMENT *is of a very high degree of Purity;* and that the Medicament itself has sometimes been erroneously held responsible for untoward effects perceived after its use, which were, however, altogether due to *impurities* resulting from inapt methods of preparation.

> [For a *parallel instance*, compare the article on "ETHYL BROMIDE MERCK," in the BULLETIN for June, 1888.—ED.]

—AMYLENE HYDRATE (also called: *Tertiary Amylic Alcohol*, *Pseudo-amylic Alcohol*, or *di-Methyl-ethyl-Carbinol*)—$C_5H_{12}O = (CH_3)_2C(C_2H_5)$-OH—is a very mobile, colorless liquid, of specific gravity 0.81, and boiling-point 100° C [212 F],—(as stated in previous BULLETIN). It is, *when pure*, *soluble in 8 parts of Water*, and is miscible with Alcohol in all proportions. Its taste is ethereo-camphoraceous, with a cooling, peppermint-like, after-sensation.

The **Physiologic action** of STRICTLY PURE AMYLENE HYDRATE, as demonstrated by Prof. Dr. J. VON MERING already in 1887 by an elaborate series of Animal-experiments (fully reported in that year's *Therapeutische Monatshefte;* July No.), exhibited the following predominant characteristics:

1.—A perfect Hypnotic effect was secured, BY APPROPRIATE DOSES, *without any greater modification of the* RESPIRATION-FREQUENCY *than that incident to Natural sleep.*

2.—The HEART-FREQUENCY and the BLOOD-PRESSURE were *not affected in any materially appreciable degree.*

3.—The effect of PURE AMYLENE HYDRATE in MEDIUM DOSES was found to be exercised principally on the *Cerebrum;*—in EXCESSIVE DOSES, however, the *Spinal chord* and the *Medulla oblongata* are affected, the Reflex actions disappear, Respiration ceases, and finally the Heart is arrested.

—The **Therapeutic uses** of AMYLENE HYDRATE, as tested by Prof. VON MERING in 60 cases, distributed over two years' Clinical practice, are summed-up in the second part of the report above quoted, as follows:

> "The total number of doses administered was 350,—varying from 3 to 5 grammes [45 to 75 grains] each. Most of the patients treated suffered from **Insomnia** as a consequence of Nervousness, Mental over-exertion, etc. Two of the patients had serious Heart-troubles.
>
> "Furthermore, the medicament was administered in *Paralysis*, *Mania*, *Delirium tremens*, and *Senile excitement;* also, in Senile, Convalescent, Anemic, Phthisical, and Febrile *Insomnias* (the latter comprising cases of Typhus and of Articular Rheumatism).
>
> "In all these cases, the medicament acted Hypnotically, *without any preliminary stage of excitement.* With the exception of only 4 instances, where the action was incomplete, the desired condition of CALM, REFRESHING SLEEP was *attained within 30 minutes*, and lasted for 6–12 hours!—CHILDREN afflicted with *Whooping-cough* had signal relief from a dose of 0.2 gramme [3 grains], taken in the evening.
>
> "In Insomnias *caused by Pain*, the action of AMYLENE HYDRATE *alone* is, like that of CHLORAL HYDRATE, *uncertain;*—in cases of this nature (as witnessed, for instance, with Ischias and in Intercostal Neuralgia), a combination of AMYLENE HYDRATE and MORPHINE was found eligible.
>
> "—UNTOWARD ACCESSORY EFFECTS *were not remarked*,—especially no Nausea nor Vomit, nor Digestive disturbance, nor Headache!
>
> "—The **Hypnotic strength** of AMYLENE HYDRATE, as relative to the size of Dose, is *intermediate between* that of CHLORAL HYDRATE and of PARALDEHYD.—That is, 2 parts of AMYLENE HYDRATE are about equal, in effect, to 1 of CHLORAL HYDRATE, or to 3 of PARALDEHYD.
>
> "—AMYLENE HYDRATE is, however, even in larger doses, *preferable to* CHLORAL HYDRATE, in view of its **Innocuousness** to the Heart and the Respiratory tract.—It is a principle, established already by SCHMIEDEBERG and his followers, that the CHLORATED DERIVATIVES of the Fat-series *act far more paralyzingly on the Heart and depressingly on the Vascular tone*, than the Halogen-free Ethers and Alcohols.—Hence, the Congestive symptoms and disagreeable sensations often noticed on the awakening from a CHLORAL-HYDRATE sleep, *are not induced by* PURE AMYLENE HYDRATE. The latter enjoys the additional preference of *not being counter-indicated by Digestive complications.*"

—AMYLENE HYDRATE may be successfully administered *by Mouth or by Rectum.* The following formulas are presented by Prof. VON

MERING,—to be modified according as large or small Doses may seem desirable:

A.—AMYLENE HYDRATE 7 grammes [5½ scr.]; Distilled Water 60 grammes [2 oz.]; Extract Licorice 10 grammes [2½ dr.];—*Take one-half* at bedtime.

B.—AMYLENE HYDRATE 5 grammes [4 scr.]; Distilled Water 50 grammes [1 oz. 5 dr.]; Mucilage Acacia 20 grammes [5 dr.];—*For Enema!*

In *Insomnias of a painful nature*, especially those from Peripheral Neuralgic pains, the following are recommended:

C.—AMYLENE HYDRATE 6–7 grammes [4½–5½ scr.]; *Morphine Hydrochlorate* 0.02–0.03 gramme [1/3 to 2/5 grain]; Distilled Water 60 grammes [2 oz.]; Extract Licorice 10 grammes [2½ dr.];—*Take one-half* at bedtime.

D.—AMYLENE HYDRATE 4 grammes [1 dr.]; *Morphine Hydrochlorate* 0.015 gramme [¼ grain]; Distilled Water 50 grammes [1 oz. 5 dr.]; Mucilage Acacia 20 grammes [5 dr.];—*For Enema!*

—In a MORE RECENT report [*Therapeutische Monatshefte*, 1889; July], Prof. VON MERING, on the strength of two years' additional Clinical experiences, adheres to the above-cited theses Nos. 1, 2 and 3 in regard to the *Eligibility* and *Perfect Innocuousness* of PURE AMYLENE HYDRATE, and also quotes *other authorities confirming them.* Among the favorable utterances thus repeated are the following:

Dr. LAVES of BETHANY HOSPITAL in Berlin says:—"Dangerous consequences were never observed. *Habituation, or decrease of effect, was not noticeable within three months' use.*—The profound and refreshing character of the Sleep induced by the AMYLENE HYDRATE was especially marked."

Dr. G. BUSCHAU, of the Sanitarium at Leubus, pronounces AMYLENE HYDRATE "an adequate Succedaneum for both CHLORAL HYDRATE and PARALDEHYD,—being preferable to the former on the ground of greater Safety, and to the latter on that of greater Agreeableness."

—Prof. VON MERING, in his second report, gives a new formula, to replace that cited under "A," above, with patients to whom the Licorice-taste is obnoxious:

E.—AMYLENE HYDRATE 7 grammes [5½ scr.]; Orange-flower Water 50 grammes [1 oz. 5 dr.]; Bitter-Orange-peel Syrup 30 grammes [1 oz.];—*Take one-half* at bedtime.

He has, however, found *the easiest way of taking* the remedy to be the following:—Stir a teaspoonful of Simple AMYLENE HYDRATE with

a wineglassful of *Beer* for several minutes; then drink the mixture off, and follow it by a mouthful of Beer alone.—(Prof. JOLLY gives it in a glass of *Wine*, to which 1–2 teaspoonfuls of Sugar are added.)—The remedy may also be administered in a few CAPSULES of 1 gramme [15 grains] contents each; to be followed by a mouthful of Water, Beer, or Wine each.

[These CAPSULES, of *Kahlbaum's own make and filling*, are obtainable in the Drug-trade.—ED.]

The regular *Hypnotical Dose* of 3–4 grammes has, by Prof. v. M., been *exceeded* in severe cases of Excitation, to run as high as 6–7 grammes [90–105 grains], *without any disagreeable consequences*, and with good action!

—The Professor furthermore invites *caution against the use of* IMPURE AMYLENE HYDRATE. He found several of the brands in the market to contain *Fusel-oil*, *polymeric forms of Amylene*, etc. Such IMPURE PREPARATIONS (which are distinguished also by *a lower degree of Solubility* than what was above stated for the Pure substance!) were found to act hypnotically also, but to engender *Congestions*, *Headaches*, *Nauseas*, and *Vomiturition*, besides.—On the other hand, the AMYLENE HYDRATE prepared by *Kahlbaum* (who employs a special, improved method of purification) was invariably found to be of ABSOLUTE MEDICINAL PURITY,—*engendering no Accessory effects whatever!*

Anemonin is the active principle of *Pulsatilla* (*Anemone P.*).—It consists of colorless, aciculate crystals, melting at 152° C [305.6 F]; *very sparingly soluble* in Water or Ether; but easily so in warm Alcohol.

According to P. Q. BRONDGEEST (*Nederl. Tijdschr. voor Geneeskd.*, 1888; p. 131), ANEMONIN is a **Cerebral poison,** whose lethal action proceeds by annihilation of the function of the Central Nervous system,—the effect being preceded and accompanied by Spasmodic and Paralytic phenomena.—This result, however, being attainable only by large doses and after a considerable lapse of time, ANEMONIN is NOT to be classified with the *Strong Poisons!*

—*Medicinally* applied, its *Daily Dose* varies from 5 to 10 centigrammes [¾ to 1½ grain], to be exhibited *in two divisions*, in POWDERS,

wrapped in Wafers.—Doses *greater* than 10 centigrammes should be *avoided;* because, already at 20 centigrammes [3 grains], Cephalalgia and Difficulty of Articulation are among the *possible* effects.

—The INDICATIONS for the administration of ANEMONIN are: **Pertussis, Bronchitis,** and **Asthma.**

Camphor, Naphtholated (*Camphorated Naphthol;* NAPHTHOL-CAMPHOR) is a syrupy liquid, possessed of remarkable therapeutic value as a **Topical Antiseptic.**

According to Dr. FERNET (*Nouveaux Remèdes*, 1889; p. 142), the diseased parts to be acted-upon should be *painted* with the liquid.—In some affections, the application is intensely *painful;* hence, the practice has been recommended, in such cases, of treating the surface with a 2-per-cent. COCAINE-solution previously to applying the CAMPHORATED NAPHTHOL; or, of adding a sufficiency of COCAINE (from 2 to 20 per cent.) to the NAPHTHOL-CAMPHOR liquid.

The action of NAPHTHOLATED CAMPHOR, when *methodically* applied, has been found to be eminently beneficial in *Furuncles*, *Coryza*, and *Angina Diphtherica;* while in *Local Stomatic Tuberculose* its effects are reported to be unparalleled.

Gold mono-Bromide (*Aurous Bromide*)—Au Br,—forming a yellowish-gray, friable mass, *insoluble* in Water,—has been made known as an **Anti-Epileptic** *of great promise* by a treatise of GOUBERT'S (in *Journal de Médecine de Bruxelles*, 1889; No. 5), which treatise has recently been awarded a prize from the BARBIER Fund by the PARISIAN ACADEMY OF SCIENCES.

GOUBERT therein recommends AUROUS BROMIDE, as being an Epileptic medicament *better borne than any other Bromine-preparation known.*

Its medium Dose FOR ADULTS is stated at 0.008 gramme [$^{12}/_{100}$ grain], gradually rising to 0.012 gramme [$^{18}/_{100}$ grain]. FOR CHILDREN, 0.003–0.006 gramme [$^{1}/_{20}$–$^{1}/_{10}$ grain].

—The MONO-BROMIDE OF GOLD was also successfully used in all varieties of *Hemicrania*, and in *Struma ecophthalmica.*

Guaiacol as the "**Sovereign Remedy in Pulmonary Tuberculosis**";—being considered *the Medicinally Active Principle of* CREASOTE.

As early as 1876, BOUCHARD and GIMBERT (*Gazette hebdomadaire de Médecine et de Chirurgie*) proposed the use of CREASOTE in *Pulmonary Tuberculosis.*

Compared with the dubious results gained by other reputed or alleged "*Specifics for Consumption,*" CREASOTE herein exhibited a certain measure of habitual success; which circumstance gradually procured for it quite an extensive application in this direction.

CREASOTE, however, is a complex substance, containing 60–90% of GUAIACOL,—with the remainder composed of the CRESOLS and other HOMOLOGUES OF VARIOUS PHENOLS.—It was, therefore, in accordance with the tendency of Modern Medicine toward the employment of *Homogeneous Substances* wherever possible, that SAHLI, of Berne, recommended **Guaiacol,**—as being **The True Therapeutic Agent in Creasote,**—to be employed in the place of CREASOTE itself!—This proposition immediately met with great favor; so that, recently, GUAIACOL has become more and more of a fixture in the *Therapy of Tuberculosis.*

—It is important that the principal physical and chemical reactions of PURE GUAIACOL should be here stated, because *only the pure substance* can be relied-upon for the *beneficent behavior* ascribed to it by the Medical reports further below quoted.

Pure Guaiacol (*mono-Methyl-catechol; Methyl-ether of Pyro-catechin*)—$C_6H_4\left\langle \begin{matrix} OH \\ OCH_3 \end{matrix} \right\}$ (1 : 2)—is a colorless, limpid, strongly refractive, oily liquid, of a peculiar aromatic odor, and specific gravity 1.1171 at 13° C [55.4 F]. It boils at 201° C [393.8 F], is soluble in 200 parts Water, and is clearly miscible with Alcohol, with Ether, and with Carbon di-Sulphide.—Its Alcoholic solution is colored *blue* by the addition of a little Ferric Chloride, and *green* by a larger addition.—One volume of GUAIACOL, with two of Petroleum Benzin, forms a *turbid* mixture; which, however, becomes *clear* (at 15° C [59 F]) on the addition of 6 further volumes of the Benzin.—One volume of GUAIACOL, with two of Soda Solution, makes a *clear* mixture, soluble

in its tenfold volume of Water clearly and without coloration:—One volume of GUAIACOL, with two of Potassa Solution, solidifies within a short time into a white, crystalline mass.

——The **Therapeutic use** of GUAIACOL as an **Anti-Tubercular** is thus detailed by recent investigators:

A. NOBILI (*Gazzetta degli Ospitali*, 1888; 76 & 77) credits GUAIACOL with two distinct powers: BOTH that of *Augmenting the Organic Power of Resistance against Tuberculous Infection*, AND that of *Destroying the Tubercular Bacilli.* Hence, Dr. NOBILI considers GUAIACOL—

"*The Sovereign of All Known Remedies in Pulmonary Tuberculosis.*"

He prefers it to CREASOTE on account of its being a *Homogeneous Substance* (having necessarily a more reliable and uniform mode of action), and, "because CREASOTE very often exhibits a *Vomitory effect!*"

Nobili's formula of exhibition is as follows:

A.—GUAIACOL 1 gramme [15 grains]; Alcohol 200 grammes [8 fl. oz.]; Tincture Gentian 25 grammes [1 fl. oz.].

At first, this mixture is given to the extent of only 5–15 drops, daily, after meals,—best to be taken in Wine, Broth, or Sugared Water.—In the combination as by the above formula, GUAIACOL is easily taken and entails no inconvenience.—*Gradually, the Dose may be increased*, up to 1, 2, and even 3 grammes [16–32–48 minims] of the Mixture per day.

All the patients treated with GUAIACOL, according to Dr. NOBILI's report, experienced an *Increase of Appetite; the Cough*, especially at night, *was decreased;* also, in some cases, *the Fever and the Night-sweats were reduced.* Generally, a distinct improvement in the Rattling sounds was noted, and the subjective feeling of the patients was markedly elevated.

—Another investigator, Dr. BOURGET (*Korrespondenzblatt Schweizerischer Aerzte*, 1889; 10), recommends the administration of GUAIACOL **in Larger Doses.**—In *Summer*, he exhibits it in VINOUS SOLUTION; in *Winter*, in mixture with COD-LIVER OIL.

The Summer Mixture is composed as follows:

B.—GUAIACOL 7.5 grammes [2 drams]; Tincture Cinchona 20 grammes [6 fl. dr.]; Malaga Wine 1000 grammes [35 fl. oz.].

Of this, 1 tablespoonful is given *at every meal* in the beginning of the treatment; which dose is *gradually increased*, up to 2–3 spoonfuls.

If, at any time, the medicament be LESS WELL BORNE THAN USUAL, its form is to be changed to that of an **Enema,** as follows:

> C.—GUAIACOL 2 grammes [30 grains]; Sweet Almond Oil 20 grammes [6 fl. dr.]; Gum Acacia 10 grammes [2½ dr.]; Distilled Water 950 grammes [2 pints];—*Make into Emulsion:* for 4 Enemas.

(THIS ENEMA should be made to go as high up as possible, being administered through a flexible tube, with the patient lying on his *left* side; sometimes it may be advantageously *preceded by* a WATER injection.)

The treatments *per os* and *per rectum* may be ALTERNATIVELY COMBINED,—the *Guaiacol Wine* being given one fortnight, and the *Guaiacol Enemas* the next.

For the Winter Treatment, this formula is directed:

> D.—GUAIACOL 3 grammes [45 grains]; Cod-liver Oil 200 grammes [8 fl. oz.].

One Tablespoonful at each principal meal is the *Internal Dose* of this, COMBINED WITH an *Outward Application*, BY INUNCTION, of the following:

> E.—Creasote 20 grammes [5 fl. dr.]; Cod-liver Oil 200 grammes [8 fl. oz.].

This Inunction is applied to *chest*, *back*, *and armpits*, at bedtime, whereupon the patient should lie well covered up to the throat.—The patient should furthermore wear, as constantly as possible, *by night and day*, a NASAL ASPIRATOR charged with 2–3 drops of CREASOTE. (This apparatus, if not readily procurable, may at need be replaced by pieces of *Rubber Tubing*, of the width of the Nares, and nearly an inch in length, into which loose rolls of *Filtering-paper* saturated with CREASOTE are introduced.)

—The treatment, as above indicated according to Dr. BOURGET, is to be continued for 3–4 months; during which time, however, the TONIC REGIMEN is not to be neglected!

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FINE CHEMICALS AND DRUGS FOR THE MATERIA MEDICA

AND THE ARTS.

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THE MYDRIATIC ALKALOIDS

of the Solanaceæ.

ALSO:

THEIR NARCOTIC AND OTHER USES;

as Hypnotics, Sedatives, etc.

A MYDRIATIC DRUG—or, briefly, a MYDRIATIC—is a medicamentous substance capable of producing **Mydriasis**, that is, a *Dilatation of the Pupil of the Eye.*

Those MYDRIATICS which have gained therapeutic prominence so far are found in plants of the Natural Order of *Solanaceæ;* and the **Active Principles** in those plants, to which their Mydriatic action is due, are certain ALKALOIDS naturally existing therein, in combination with Vegetable Acids, and separable therefrom by chemical processes. Thus are obtained: ATROPINE from *Atropa belladonna;* HYOSCYAMINE from *Hyoscyamus niger;* etc., etc.

Chemistry enables us to distinguish, among the SOLANACEOUS MYDRIATIC ALKALOIDS, the class of

Homogeneous, or Simple, Bases,

—such as: ATROPINE, HYOSCINE, HYOSCYAMINE CRYSTALLINE,

—from the class of

Heterogeneous, or Mixed, Bases,

—such as: DATURINE COMMERCIAL, DUBOISINE, HYOSCYAMINE SYRUPY, SCOPOLEINE;

—which latter class comprises *Natural Mixtures* of the Simple Alkaloids of the first class, in such ratio of mutual strength as that in which they are naturally found present together in various plants,—as in *Datura stramonium*, *Duboisia myoporoides*, *Hyoscyamus*, *Scopolia japonica*, etc.—(To the HETEROGENEOUS class, likewise, probably belongs the newly discovered Mydriatic Base MANDRAGORINE, from *Mandragora vernalis.*)

—The **Homogeneous, or Simple, Mydriatic Alkaloids,** as far as they are known, and as enumerated above, are all possessed of one common Empiric Formula:

$$C_{17}\,H_{23}\,N\,O_3;$$

that is, *they are mutually isomeric;* and the chemical distinction between them is based principally on the different forms and behaviors of their Double Salts with the Heavy Metals, and partly of their Fractional Derivatives.

—*Besides the* **Natural Solanaceous Alkaloids,** as above-named, an ARTIFICIAL MYDRIATIC SIMPLE ALKALOID, procured by Synthesis from Mandelic Acid and Tropine (a fractional derivative of ATROPINE), is in good Therapeutic use. This is

$$\text{HOMATROPINE} = C_{16}\,H_{21}\,N\,O_3;$$

—which formula shows it to be a HOMOLOGUE of Atropine, Hyoscine, and Hyoscya-

mine,—the three SIMPLE ALKALOIDS above discussed; and this close chemical relation is more than equaled by its Physiological similarity to them, which entitles it to be discussed along with the NATURAL SOLANACEOUS MYDRIATICS.

—The latest chemical researches have established the probability that the three ISOMERIC MYDRIATIC ALKALOIDS—Atropine, Hyoscine, and Hyoscyamine—are *more closely related*, even, than what the mere condition of *"Isomerism"* would necessitate. With ATROPINE and HYOSCYAMINE, this seems to be a settled fact.

[Whether *"Polymerism"* be here involved, has not yet been ascertained.—ED.]

Thus, it has been known for a length of time, that *both* ATROPINE *and* HYOSCYAMINE may be obtained from *Atropa belladonna*,—according to the different processes of extraction and isolation employed. Furthermore, SCHMIDT and WILL have established the possibility of *converting* the HYOSCYAMINE, gained from *Atropa belladonna*, into ATROPINE by keeping it for some time at a temperature above its melting-point, or by treating it with a small quantity of Alkali.

—*But, notwithstanding the gradual weakening of the Distinctive Limits drawn between these Alkaloids* BY CHEMISTRY, *the Differences hitherto found between them* BY PHYSIOLOGY, *and, consequently*, BY THERAPY, *are not only fully maintained, but also intensified, by recent research*,—as will be apparent even from their following brief preliminary characterizations.

The administration of ATROPINE is often counter-indicated by a frequently arising *Idiosyncrasy* against this medicament; also, a peculiar variety of *Conjunctivitis* is occasioned by ATROPINE; furthermore, *Toxic symptoms* of severest degree are quite liable to supervene in ATROPINE medication.

DUBOISINE and DATURINE act very much *like Atropine*, only somewhat *more strongly;* yet they are favored as SUCCEDANEA FOR ATROPINE, whenever *Idiosyncrasy* against the latter prevails.

Pure HYOSCYAMINE is, according to late investigations by GNAUCK, *less toxic than Atropine*, which it resembles otherwise in the general *direction* of its effects; a characteristic difference which distinguishes it from Atropine, however, consists in its acting, *in small doses*, as a **True Hypnotic.**

HYOSCINE likewise gives the *Atropine effects;* but *its action is prompter* than that of Atropine, and is *not followed by such dangerous general symptoms* as those frequently consequent on Atropine medication. HYOSCINE is, moreover, *like Hyoscyamine*, **an excellent Hypnotic.**

HOMATROPINE, in the general *direction* of its effects, *corresponds entirely to Atropine*,—enlarging the Pupil and paralyzing the Accommodation, as Atropine does; but it *differs essentially* from Atropine in the *Course* of its MYDRIATIC effect, which, while being characterized in its *Maximal period almost exactly like* that of Atropine, exhibits a *very considerably briefer Continuance* than the Atropine effect.

In what follows, the **Mydriatic Solanaceous Alkaloids** principally used in Therapy: ATROPINE, HOMATROPINE, HYOSCYAMINE, and HYOSCINE,—will be treated separately, with especial regard to their *Therapeutical and Pharmacological* points of interest, in various directions **besides** that of **Mydriasis.**

1.—Atropine.

Pure Atropine Alkaloid appears in fine, silky, colorless and odorless needles of bitter-acrid taste; melts at 113.5° C [236.3 F]; *dissolves* in 200 parts cold or 54 of boiling water, in 2 1/2 of 90-% Alcohol, in 60 of Ether, very easily also in Chloroform and in Amylic Alcohol.—Its *Aqueous Solution* undergoes rapid change by contact with air; it becomes yellow and assumes a disagreeable odor,—without, however, losing its Toxic character.

The Uncombined Alkaloid Atropine is *very little employed* in Medicine; its *Salts*, especially the Sulphate, are used instead.

— Atropine Sulphate

$$-(C_{17}H_{23}NO_3)_2 . H_2SO_4 -$$

is color- and odor-less, *neutral; easily soluble* in Alcohol and in Water, less so in Ether.—It contains 85 1/2 % of Atropine.

—Atropine Sulphate Solution is exhibited by Instillation: for facilitating Ophthalmological Examinations in *Keratitis*, *Iritis*, *etc.;* for preventing *Prolapsus of the Iris* in Perforations; in the Disruption of *Synechias;* and in other Ophthalmological Operations.

Subcutaneously, it is exhibited in *Neuralgias* and in *Phthisical Nocturnal Sweats*, also in *Ptyalism.*

Internally, it is exhibited in *Epilepsy*, *Nervous Asthma*, and *Cardialgy.*

Official Maximal Internal Dose:

Single 0.001 gramme [1/64 grain]; *Daily* 0.003 gramme [1/20 grain].

Standard Formulas:

1.—*Solution for Ophthalmological Instillation.*

Atropine Sulphate 0.01–0.05–0.08 gramme [1/6–3/4–1 1/4 grain]; Distilled Water 10 grammes [2 3/4 fl. dr.].

2.—*Pills, in Phthisical Night-Sweat.*—[By Fräntzel.]

Atropine Sulphate 0.01 gramme [1/6 grain]; Glycyrrhiza Powder 2.5 grammes [38 grains]; Glycyrrhiza Extract 0.5 gramme [8 grains];—Make 20 Pills; dust with Lycopodium.—*One Pill at bed-time!*—(Each Pill contains 0.0005 gramme [1/120 grain] of Atropine Sulphate.)

3.—*Hypodermic Solution.*

Atropine Sulphate 0.01 gramme [1/6 grain]; Distilled Water 10 grammes [2 3/4 fl. dr.].—1/4–1/2 *Syringeful* (at 16 minims per Syringe) *to be*

injected subcutaneously!—(Each Syringeful contains 0.001 gramme [1/64 grain] of Atropine Sulphate.)

—Extensive use is made also of **Atropine Valerianate** and of **Atropine Borate.**—The indications and effects are *the same* as with ATROPINE SULPHATE.

The BORATE is employed *only in Ophthalmo-Therapy.*

Formula for the Valerianate.

4.—*Mixture, in Whooping-cough.*—[By MICHÉA.]

ATROPINE VALERIANATE 0.001 gramme [1/64 grain]; Infusion Linden-*leaves* 120 grammes [4 fl. oz.]; Syrup Tolu 20 grammes [4 fl. dr.].—*One Teaspoonful every half hour!*

—ATROPINE and its SALTS may occasion *Grave Symptoms of Poisoning, and even Death,* in doses of 0.01–0.06 gramme [1/6–1 grain]; while, on the other hand, *Recovery* has been witnessed after doses of 0.25–0.5 gramme [4–8 grains]!—The **Toxic Action** of ATROPINE is manifested principally in a considerable *Dilatation of the Pupils, Increase of the Heart-frequency, Diminution of the Glandular Secretions* (whence a Parching and Burning in the Pharynx!), *Paralysis of the Intestines,* and *Diminished Excitability of the Sensor Nerve-ends.*

—The **Antidotes** used in *Atropine Poisoning* are: EMETICS (APOMORPHINE HYDROCHLORATE 0.005–0.01 gramme [1/12–1/6 grain]);—likewise: CHLORAL HYDRATE, 3 grammes [45 grains], several times *repeated;*—and, also: PILOCARPINE, *subcutaneously,* 0.02 gramme [1/3 grain], *repeated* a number of times.

[TO BE CONTINUED.]

Adonidin—a GLUCOSIDE containing 42.6% of Carbon, 7.5% of Hydrogen, and no Nitrogen—is the medicinally active substance in *Adonis vernalis.*

The opinions as to its PHYSIOLOGIC ACTION having hitherto been at variance, N. GERGIEJENKO, of Kasan, (*Gaz. Lek.,* 1888; VIII, 32) instituted a new series of experiments with it, which show that ADONIDIN acts on *Cold-blooded* animals as a *Heart-poison;* while in *Warm-blooded* animals it acts toxically on the **Medulla oblongata.**

ADONIDIN appears as a *hygroscopic,* yellowish-white powder, *readily soluble* in Water and in Alcohol; insoluble in Ether, Chloroform, and

Benzene. (When heated over 90° C [194 F], it is transformed into a blackish-brown mass.)

— The use of ADONIDIN is indicated wherever *Herba Adonidis* has been found eligible. It is therefore prescribed in **Heart-troubles,**— acting therein more **by Diuresis** than through the Heart itself.

The *Single Dose* of ADONIDIN—or, preferably, of **Adonidin Tannate**—should be of 0.005 gramme [$^1/_{12}$ grain] in a PILL. The *Daily Dose should not exceed* 1–2 centigrammes [$^1/_6$–$^1/_3$ grain],—in order to avoid Vomit, Gastric disturbance, and Nervous affection.

Eserine and Eseridine.—Last year's *Pharmazeutische Zeitung*, in No. 65, and *Berliner Thierärztliche Wochenschrift*, in No. 40, published reports by the Veterinary Surgeon W. EBER, of Berlin, on "Physostigmine and a New Derivative thereof." These reports gave a very minute description of a new substance discovered by EBER, as being derivable from PHYSOSTIGMINE (ESERINE), and by him called "ESERIDINE," which was prepared by BOEHRINGER in a crystalline form.

IT WAS CLAIMED, in those reports, that the newly-discovered substance partakes ONLY of the *therapeutically useful*, but NOT of the *obnoxious and dangerous* properties of ESERINE. Particular stress was laid on its being only *one-sixth as toxic* as ESERINE; "in consequence whereof, much larger doses could be administered without endangering the animal's life";—and, thus, a *Safe Subcutaneous Veterinary Cathartic* was supposed to have been found! — These views were propagated and advertised with so much vigor as to attract very marked attention in Pharmacological and Veterinary circles.

—A rather unfavorable view has been taken of that new substance, ESERIDINE, by DIETRICH SCHWEDER, of Professor KOBERT'S Pharmacological Institute, connected with DORPAT UNIVERSITY.— Having conducted a series of thorough clinical investigations of it, he writes:

> "The experiences I gathered will not allow me to concede to ESERIDINE any advantages whatever over ESERINE. The circumstance which most markedly impedes the therapeutic usefulness of the CALABAR ALKALOIDS consists in the ready *susceptibility of the Heart* to their action. With Subcutaneous application, their effect reaches the Heart before it becomes ap-

parent in the *Intestinal contractions;*—and this drawback *is common*, **in like degree,** *to both the Alkaloids:* ESERIDINE and ESERINE.

"Nor am I in a position to say that the *Inflammative Symptoms* in the *Intestinal and Gastric Mucous membrane*—as far as any such appear—had shown more or less strongly with either the one or the other of the two Alkaloids. This is purely dependent on the quantities of the respective medicaments injected. **A *relatively* equal-sized Dose of the Eseridine acts, herein, exactly like one of Eserine.**

"**Hence,** the assertion, put-forth in certain quarters, *that Eseridine is free from the toxic action of Eserine*, **is false.** The TRUE STATEMENT would be this:

"Eseridine acts qualitatively like Eserine, but in sixfold weaker degree.

"—Therefore, the value of the comparatively expensive ESERIDINE for Therapy may be pronounced equal to zero!—If it should prove practicable *as a Cathartic for Herbivorous Animals*,—which I am not inclined to deny,—**the same effect will be realizable by Eserine in Doses sixfold smaller.**

"—Whether an *Internal Administration of* ESERIDINE *to* HUMAN PATIENTS, **in Constipation,** in its character of a SLOWLY-SOLUBLE SALT, may prove advisable, can neither be denied nor affirmed on Theoretical grounds; but this use of it *still needs indorsement* by an exact course of Clinical experiment."

—Thus far, SCHWEDER'S report!—I myself presume it will be safe to expect *no eminent distinction* to be achieved by ESERIDINE in Veterinary Practice; *especially so*, since **Eserine-Pilocarpine,** that excellently-active combination of ESERINE with PILOCARPINE, described in the BULLETIN for January of the present year, has manifested *such extraordinarily beneficial action!*

Hemoglobin (*Hæmoglobin*) is the principal and most characteristic constituent of the red corpuscles of the Blood of man and other vertebrate beings. It performs the essentially vital function,—in the processes of circulation and respiration,—of bearing the waste gases of the organism—especially Carbon Di-oxide—to the lungs and exchanging them for Oxygen, which it then bears to the various tissues and organs of the body. It is at the same time the bearer of the *color* of the Blood,—containing, as it does, **all the Iron** present in the Blood.

HEMOGLOBIN, as isolated from the Blood, appears in the form of a reddish-brown powder of peculiar odor; it is *readily soluble* in Water, to which it communicates a red-brown tinge.

The chemical form and combination in which IRON exists in HEMOGLOBIN is thought to be such as to make the IRON **particularly easy of Assimilation** into an organism to which HEMOGLOBIN is given *by the Stomach.* Hence, the use of HEMOGLOBIN **as a Chalybeate,** or Iron-bearing Medicament, has been attempted in cases of disease where *an Atonic condition of the Digestive tract* impedes the assimilation of medicines; notably, in certain cases of *Anemia* and of *Chlorosis.*

Formulas (by DESCHIENS):

A.—HEMOGLOBIN 190 grammes [6 oz.]; Syrup sufficient to make 1 liter [33 1/2 fl. oz.].—*Two to four Tablespoons per day*, for Adults (half as much for Children)!—[*Each Tablespoon* contains 2.85 grammes—or 43 grains—of HEMOGLOBIN; corresponding to 0.0123 gramme, = 0.19, or nearly 1/5, grain, of METALLIC IRON.]

B.—HEMOGLOBIN 150 grammes [4 3/4 oz.]; Rich White Wine sufficient to make 1 liter [33 1/2 fl. oz.].—*Two and one-half to four Tablespoons per day*, for Adults (half as much for Children)!—[*Each Tablespoon* contains 2.25 grammes—or 34 grains—of HEMOGLOBIN; corresponding to 0.00975 gramme, = 0.15, or 3/20, grain, of METALLIC IRON.]

—Some persons being susceptible to the HEMOGLOBIN odor, it has been deemed advisable to exhibit the medicament, in these cases, in *Sugar-coated Pills*, flavored with PEPPERMINT-OIL. The following formula is then eligible:

C.—HEMOGLOBIN 25 grammes [6 1/2 dr.]; Milk-sugar 5 grammes [4 scr.]; Peppermint-oil 3 drops; Acacia-mucilage sufficient to make Pill-mass;—Make 100 Pills, *sugar-coated.—Six to Twelve Pills per day*, for Adults (half as many for Children).—[*See:* "PILL-TAKING MADE EASY,"—next page!]

—The various formulas above noted, for administering HEMOGLOBIN, *have been tested* in several of the Hospitals at Paris, France, for over a year past,—*with exceedingly favorable results!* In cases of well-defined **Chloroso-Anemia,** the weekly enumerations of the RED BLOOD-CORPUSCLES showed *a gradual increase of their number*, bringing it from 400,000 up to 500,000 per cubic millimeter.

—*A special virtue* of HEMOGLOBIN, as compared with other CHALYBEATES, is, that it is **not an Anexosmotic,** and consequently *does not constipate* the patient.

Pill-taking Made Easy!—In regard to the above-given formula "*C*" for HEMOGLOBIN, it may be well to recall an expedient calculated *to relieve the difficulty* which many patients experience in attempting **to swallow a pill**—especially if it be a large one.—ASTHALTER (*Medical and Surgical Reporter*, 1885) suggested that the difficulty can be entirely obviated *by placing one or more of the Pills* UNDER THE TONGUE, *and then swallowing a draught of Water*, which INVOLUNTARILY and almost UNNOTICEABLY draws the Pill or Pills with it!

Thiocamph, — a New Disinfectant. — J. EMERSON REYNOLDS (*Chemical News;* 59: 291) made the discovery that, by the action of SULPHUR DI-OXIDE gas on CAMPHOR, without the application of any pressure, *a liquid is formed*, to which the above name has been given. THIOCAMPH possesses the remarkable property that, bottled in the usual way, it can be *preserved unchanged* at ordinary temperatures; but that, exposed to the air in a thin film, it *gives-off enormous volumes* of SULPHUR DI-OXIDE gas (so-called "*Anhydrous Sulphurous Acid*"). **This same remarkable behavior** shown by the SULPHUR DI-OXIDE — thus being bound, or quiescent, in the CAMPHOR-compound, as long as it is confined in a corked vessel, and being liberated in abundance, and diffused through the atmosphere, when exposed—extends also to certain **other Bactericidal substances** when incorporated with the THIOCAMPH liquid.—Thus, a means is provided of carrying *not only "Sulphurous Acid" gas, but other Disinfectants, combined or mixed with it*, into and throughout the atmosphere of a room, cellar, or any other inclosed space,—the gases or vapors being *evolved from a liquid conveniently portable in a bottle!*—The contents of a *six-ounce* bottle, spread out in a very attenuated stratum, are capable of evolving more than 1250 cubic inches (about $5^1/_2$ gallons) of SULPHUR DI-OXIDE (Sulphurous Oxide or "Acid" gas).

One Ounce of THIOCAMPH, shaken-up with a Quart of Water, makes a good *Disinfecting Liquid for Sprinkling* over infected objects.—One Ounce to one Gallon makes a good *Disinfecting Liquid for Soaking* clothes.—The *residual odor* of THIOCAMPH, remaining after the process, is agreeably aromatic.

STRAY ITEMS.

No. 4.

MERCURY, GREEN AND YELLOW IODIDES.

There appears to be some possibility of *these two salts* being confounded, from the following circumstances:

"GREEN IODIDE OF MERCURY (*Hydrargyri Iodidum viride*)" of the U. S. Pharmacopœia is, in some countries, known also as "YELLOW Iodide of Mercury (Hydrargyrum jodatum *flavum*)". Its color, *when recently washed* with Alcohol, is *more of yellow* than of green, although a greenish cast is always discernible in it; the *green* tint then gradually becomes stronger and darker—even to blackness—with age, and *especially with exposure* to atmospheric moisture and to light.—Its formula is:

$Hg_2 I_2$—(*Proto*-Iodide).

—The *real* YELLOW *Iodide of Mercury*, whose color is, when fresh, that of a perfectly pure, bright *Chrome yellow*, is a *more stable* compound than the *Green* (or *so-called* "Yellow") Iodide, and consequently also retains its yellow color much more tenaciously. Still, on prolonged exposure it also darkens and deepens in color finally, with an unmistakable cast of green superadded.—The formula of this *non-officinal* salt is:— $Hg_4 I_6$—(*Sesqui*-Iodide).

AMERICAN PUBLIC HEALTH ASSOCIATION.

The SEVENTEENTH ANNUAL MEETING of this Association, combined with a SANITARY EXHIBITION, will be held at BROOKLYN, N. Y., (Hall of the BROOKLYN INSTITUTE, corner of Washington and Concord Streets) from October 22nd to 25th, this year.—The EXHIBITION HALL will be at the Northwest corner of Fulton and Pineapple Streets, one block from the Meeting Hall. The Exhibition will continue from Oct. 22nd to Dec. 1st. (*Admission free.*)

Detailed Information will be sent on application to the Chairman of the Executive Committee: J. H. RAYMOND, M.D., 173 Joralemon Street, BROOKLYN, N. Y.

MERCK'S BULLETIN

A Periodical Record of New Discoveries, Introductions, or Applications of Medicinal Chemicals.

Moved by Professional — not Business — Interest.

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1889.

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By E. MERCK.

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NEW MERCURY COMPOUNDS

for Subcutaneous Syphilidology.

Mercuro-Phenolides and Mercuro-Phenolide Double Salts.

Soon after the MERCURIAL METHOD in SYPHILIDO-THERAPY had been amplified by the adoption of **Hypodermics**, the tendency was made manifest, toward having *a greater choice of Mercurial preparations that are adapted for Subcutaneous exhibition.*

Among the Mercurial compounds introduced for this purpose, *one class* is distinguishable by READY SOLUBILITY in the Animal Fluids, and, in consequence, by RAPID ABSORPTION into the Organism; while *another class* is noted for its SLOW SOLUBILITY, and for its consequent **Double Mode of Action**,—*combining the advantages of* **Acute** (Initial, or Primary), with those of **Chronic** (Subsequent, or Secondary), **Mercurialization.**

Prominent in the latter class are the **Mercuro-Phenolide Double Salts**,—a peculiar series of combinations recently prepared by me.

—Before discussing *these new* MERCURO-PHENOLIDE DOUBLE SALTS, I shall, in order *to guard against erroneous substitutions*, give brief mention also to those SIMPLE MERCURO-PHENOLIDES which had already before been put to Therapeutic use.

> [The name "MERCURO-PHENOLIDES" is here given to combinations of MERCURY with the various PHENOLS (that is: with *Nucleal* Hydroxyl-derivatives of the Aromatic Hydrocarbons),—whether formed *by Addition or by Molecular Substitution.*—ED.]

I.—SIMPLE MERCURO-PHENOLIDES.

Mercury Phenate (Carbolate), [*Mercuro-Phenol*],—according to Schadeck.—The MERCURY PHENATES were introduced into Therapeutics by GAMBERINI.—The particular modification of MERCURY PHENATE produced as a *Precipitate* by the reaction between solutions of Mercury bi-Chloride and of Sodium Carbolate is the one known by the name of SCHADECK, its originator.—According to the conditions governing the process of precipitation, *more or less basic* products are obtained,—distinguishable by their colors, which vary *from grayish-white to yellow and to orange.* [Accordingly, these products are of **varying Mercury-**

strength,—a circumstance which stands in the way of Exact Dosage.—Nevertheless, *very favorable results* are said to have been attained with this preparation as an Anti-Syphilitic by Hypodermics! [*See remark* on "Intramuscular Injections,"—below!]

Note.—Mercury Phenate is not to be confounded with the so-called "*Phenolide Double Salts*" (as described further below), to wit: Mercury Phenol-Acetate [*Merck*], Mercury Phenol-Sulphate, etc.; which present a *white, crystalline* appearance.

Mercuro-Thymol (*Thymol-Mercury;* or: *Mercury Thymate*) has, in England, been recommended for Therapeutic use (*Medical Standard*, 1888; July).—It is, like the above-described Phenate, a *Precipitate*, and is similarly obtained from the solutions of Sodio-Thymol and of Mercuric Nitrate. Its color is described as "*purplish green.*" Lallemand (*Annales de la Chimie et de la Physique*, III; 49: 148) ascribes to it the composition:

$$C_{10} H_{13} . Hg . O H.$$

This basic compound is charged with the drawback of *lacking permanence.*

Note.—Mercuro-Thymol should not be confounded with the "*Phenolide Double Salt*": Mercury Thymol-Acetate [Merck]; which has quite a different composition (see "Mercur-Thymol Salts," in last January's Bulletin; and "Mercuro-Phenolide Double Salts," further below!), and which is *very permanent, well crystallized, and white.*

Mercuro-beta-Naphthol (*beta-Naphthol-Mercury*) is highly extolled by E. Bombelon (*Pharmazeutische Zeitung*, 1888; No. 98, page 739) for its very beneficial action, Externally, in *Old Sores and Wounds, Eczemas, Herpes;* also, Internally, in *Typhus.*

It is a *lemon-yellow powder* (which, however, is said by Bombelon to be capable of crystallization). It is devoid of odor and taste, and is insoluble in the common solvents. The method of its preparation, and its composition, have not been published.

Note.—Mercuro-beta-Naphthol is, however, different in its composition from that of the "*Phenolide Double Salt*" (already described in Bulletin for April, 1889): Mercury beta-Naphthol-Acetate [Merck]; which comes as a *white* powder consisting of minute *crystals.*

II.—MERCURO-PHENOLIDE DOUBLE SALTS [*MERCK*].

These COMPOUND PHENOLIDES *are distinguished* from the various SIMPLE PHENOLIDES of Mercury—as above instanced—by showing *a clear crystalline form*, and by their CHEMICAL COMPOSITION, which embraces, **besides Mercury and a Phenol** (that alone constitute the *Simple* Mercuro-Phenolides), **also an Organic or Inorganic Acid** as an essential Molecular Constituent.

> I have, therefore, described these COMPOUND MERCURO-PHENOLIDES, briefly and superficially, as "*Double Salts* of Mercuro-Phenolides", that is, as *Compounds of Mercuro-Phenolides with Mercury-salts of the Organic or Inorganic Acids;* although their chemical constitutions have not yet been exactly determined.
>
> Thus, the tentative formula:
>
> $$C_{10}H_{13}O\,Hg - Hg\,CH_3CO_2,$$
>
> for MERCURY THYMOL-ACETATE (see BULLETIN for January, 1889),—was given by me, under reserve, *not* as necessarily indicating a *Mercurous* compound; but simply as expressing the fact that, according to the results of Analysis, the simplest assumptive construction for this compound would be that it is a Substitutive Combination of *One half-Molecule of* MERCUROUS ACETATE *with One Molecule of* MERCUROUS THYMATE (Mercuro-Thymol; Thymol-Mercury).

—Of such MERCURO-PHENOLIDE DOUBLE SALTS, the following have so far been introduced:

Mercury Phenol-Acetate [Merck], *a well-crystallized salt*, which appears in minute, *colorless* needles, aggregated into spheroidal conglomerations. In its remaining qualities it *much resembles* the THYMOL-ACETATE, next below mentioned.

> [*It must not be confounded* with MERCURY PHENATE, acc. to SCHADECK,—an amorphous, grayish or yellowish powder, as above described under "*Simple* Mercuro-Phenolides".]

Mercury Thymol-Acetate [Merck], *a very distinctly crystalline salt* of constant composition and quite *permanent character; white*, odorless and tasteless; whose **Therapeutic Virtues** have been already quite largely demonstrated.—(*See:* "MERCUR-THYMOL SALTS" in BULLETIN for Jan., 1889!)

[*Not to be confounded* with MERCURO-THYMOL, acc. to LALLEMAND,—a colored, amorphous-looking powder, as above described under "*Simple* Mercuro-Phenolides".]

—*Similar* to MERCURY THYMOL-ACETATE [MERCK] are the following:

Mercury Thymol-Nitrate;
Mercury Thymol-Sulphate.

Mercury beta-Naphthol-Acetate [Merck], recently prepared as a *white, crystalline* substance, which, in its various properties, is *very much like* the THYMOL-ACETATE and PHENOL-ACETATE of MERCURY, above described.—(*Compare*, for a statement of various uses of it, a description of its *older*, amorphous form, as given under "MERCUR-BETA-NAPHTHOL-ACETATE [MERCK]", in BULLETIN for April, 1889 !)

[This preparation *should be distinguished* from BOMBELON'S MERCURO-BETA-NAPHTHOL,—a yellow, amorphous powder, as above described under "*Simple* Mercuro-Phenolides."]

—Besides the DOUBLE SALTS OF MERCURY WITH MONO-HYDROXYLIC PHENOLS,—just described,—I have also prepared a few others, some of which are *yellow*, from PHENOLS of the same class ;—for instance,—

Mercury alpha-Naphthol-Acetate;
Mercury tri-Bromo-phenol-Acetate.

—Some of the DI- and the TRI-HYDRIC-PHENOL DOUBLE SALTS OF MERCURY have likewise been produced by me ;—for instance,—

Mercury Resorcinol-Acetate;
Mercury Phloro-glucinol-Acetate;

—the former of which is also *yellow*.

——Whether all these DOUBLE SALTS OF MERCURO-PHENOLIDES show *individual differences* in their Therapeutic actions; and whether any of them be entitled to *preference over the others* in Medicinal use,—has not yet been established by sufficient Clinical experience.

But this much can be affirmed to-day *with certainty :* that the

MERCURY THYMOL-ACETATE,

which is the one of them *most largely tested* in Clinical and Hospital Practice so far, has, *in every place and instance where it was tried*, **given exceedingly happy results!**

Since the first description of MERCURY THYMOL-ACETATE appeared in these columns, two further medical authorities of prominence have especially contributed toward a still more exact therapeutic knowledge of *this class of Mercury preparations.*—One of these contributions, by Prof. NEISSER, of Breslau, is particularly mentioned below, under "INTRAMUSCULAR INJECTIONS"; the other, by Dr. WELANDER, of Stockholm, (which was communicated to me privately), states that the doctor's extensive therapeutic experiments with MERCURY THYMOL-ACETATE were throughout crowned by very gratifying successes!

Even at this early day, therefore, the assertion can confidently be made, that *the introduction of* **Thymol-Mercury Compounds** *in* **Anti-Syphilitic Therapy** *constitutes a signal accession to the* MATERIA MEDICA; and that the success already compassed by some members of the above-described class of

INSOLUBLE MERCURY COMPOUNDS

—(*see, also:* "INTRAMUSCULAR INJECTIONS", below!)—

offer both ample warrant and motive for *a thorough experimental study* of the remaining MERCURO-PHENOLIDES.

Intramuscular Injections *of Insoluble Mercury Compounds* in Syphilis.

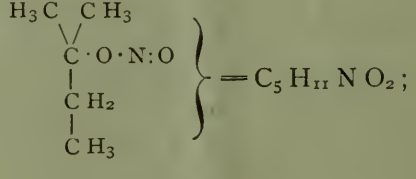
This is a mechanically and topically peculiar method of **Hypodermic** exhibition of MERCURY-SALTS *of difficult solubility* in Syphilitic affections; which has been cultivated and developed,—*with remarkably satisfactory results* **both for Efficacy and Safety,** and for **Convenience of Treatment** likewise,—by Drs. JADASSOHN and ZEISING, of Prof. NEISSER'S CLINIQUE at BRESLAU UNIVERSITY, (as *described in detail* on page 6 of the BULLETIN for January, 1889!).

This method, as applied to *Insoluble* (or Difficultly Soluble) *Mercury-compounds*, has shown, by its results, that **the advantages of Both Acute and Chronic Mercurialization are combined** by a properly-made injection of such compounds,—the Resorption of the Metal from the injected region

proceeding rapidly in the period immediately following the operation, and *more slowly* later-on.

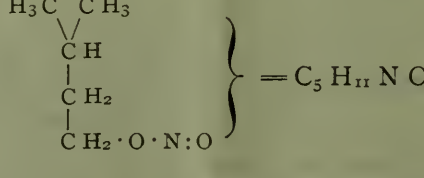
—Prof. NEISSER himself has recently published an elaborate comparative review "ON THE VARIOUS MERCURIAL METHODS OF SYPHILIDOLOGICAL THERAPY", (*Klinisches Jahrbuch*, 1889; I); in which he recommends the method of **Intramuscular Injection**, as practiced by JADASSOHN and ZEISING with **Mercuro-Thymol Double Salts**, as having proved *efficient and eligible in every case.*

Amyl Nitrite, Tertiary [!], ("AMYLENE HYDRO-NITRITE"; *Nitrous Ester of Amylene Hydrate;* **Bertoni's Amylo-nitrous Ether**).—This *new* Amyl compound, intended as a **Desirable Succedaneum for the Ordinary Amyl Nitrite** (*Iso-Amylic Nitrite; Nitrous Ether of Fermentation-Amyl Alcohol;* "FUSEL-OIL NITRITE"), has been devised by BERTONI, Professor of Chemistry at PAVIA UNIVERSITY. Its constitution answers to its production from **Tertiary Amylic Alcohol** (*di-Methyl-Ethyl-carbinol; Amylene Hydrate*), and is represented by the following formula:



$= C_5 H_{11} N O_2$;

—while the OFFICINAL (U.-S.-Ph.), or ORDINARY, AMYL NITRITE, being prepared from *Iso-amylic Alcohol*, has the formula, **isomeric** with the above, of:



$= C_5 H_{11} N O_2$.

TERTIARY AMYL NITRITE has a weak camphoraceous, not disagreeable odor, and a peppermint-like taste. It boils at about 30° C [86 F]. With the addition of a trifle of *Anhydrous Sodium Nitrate*, it may be preserved undecomposed for a long time.

According to investigations by BALP and BROGLIO (*Bolletino Farmaceutico*, 1888; July, p. 193) the **Physiologic action** of TERTIARY AMYL

NITRITE is the *same in kind* as that of ISO-AMYL NITRITE, but *somewhat stronger in degree, and more enduring.* It also admits of **Larger Doses** being taken, BY INHALATION, *without danger.*—The *disagreeable subjective sensations*, the Throbbing in the Temples, etc., entailed by the use of the ORDINARY AMYL NITRITE, are reported *to be wanting* after the use of BERTONI'S TERTIARY Ether. Hence, it is inferred that the new preparation is *free from any Specific Danger* in cases complicated with *Heart-weakness!*

Given by INHALATION, it is followed by a half hour's refreshing sleep.

—INTERNALLY, it is given—in the same classes of complaints where the ORDINARY AMYL NITRITE is eligible—in doses of 5–20 drops, on Sugar (wrapped in a Wafer, if desired), or in Gelatine capsules.

—SUBCUTANEOUS INJECTIONS can be made of TERTIARY AMYL NITRITE, by dissolving it in *Watery Glycerin.*

Caffeine, associated with Hypnotics, in Heart-troubles.—Some time ago already, the researches of SCHRÖDER had demonstrated that the administration of CAFFEINE, in conjunction with PAR-ALDEHYD and CHLORAL HYDRATE, in dogs and rabbits, *largely augments the Urine Secretion.*

The recent investigations of V. CARELLO and CARUSO-PECOSARO (*Annal. di Chim. e Pharmacol.*, 1889; April, p. 255) confirm and amplify those observations also in regard to healthy and convalescent *Human* beings. They show, in addition, that the combination above mentioned, *in Heart-patients*, besides causing **Increased Diuresis,** also *regulates the functions of the Heart and Vessels.*

—These two investigators, however, on the strength of their observations, recommend that, in ORGANIC HEART-DISEASE, no CHLORAL HYDRATE, but *only* PAR-ALDEHYD be used in conjunction with the CAFFEINE; because PAR-ALDEHYD is much milder in its action on the Heart than CHLORAL HYDRATE.

Santonin-oxim,—reported to be a **Non-Toxic Succedaneum for Santonin.**

[ACET-OXIMS are *Iso-nitroso-derivatives* of ALDEHYDS or of KETONES, or of combinations containing a *Ketone-group*. They are obtained by the addition of HYDROXYL-AMINE, or of a HYDRAZINE, to the ALDEHYD or KETONE or its compound, and the splitting-off of H_2O.—Hence, they are characterized by the group "$:N\cdot OH$",—called the OXIM-group.—ED.]

SANTONIN-OXIM was prepared by CANNIZARO, by the action of HYDROXYL-AMINE HYDROCHLORATE on an *Alkaline Solution* of SANTONIN.

[In this reaction, the Oxygen-atom of the *Ketone-group* in the SANTONIN enters the HYDROXYL-AMINE, splitting off a Water-molecule therefrom, and thus forming, as a remnant, the OXIM-group.]

$$\underset{\text{[Santonin.]}}{C_{15}H_{18}O_3} + \underset{\text{[Hydroxyl-amine.]}}{NH_2OH} = \underset{\text{[Water.]}}{H_2O} + \underset{\text{[SANTONIN-OXIM.]}}{C_{15}H_{18}O_2NOH}.$$

—According to COPPOLA (Répertoire de Pharmacie, 1889; 45 : 257), SANTONIN-OXIM is a well-crystallizable substance, and is *far less easily soluble in the animal fluids* than SANTONIN. While being *Non-toxic*, it is reported to be *just as efficacious* an **Anthelmintic** as SANTONIN, when given in about THE THREEFOLD DOSE of the latter.

—This remarkable fact is explained as follows:—**The Vermifugal Santonin-action** *is not in any wise dependent on an absorption of the medicament by the Human Organism*, because the action is to be exercised DIRECTLY on the LUMBRICS (Worms) extant in the Intestinal canal, *during the passage of the undissolved medicament* through that canal.—NOW, SANTONIN sometimes occasions toxic symptoms in the patient, by first inducing an *Intestinal Catarrh* accompanied by an inordinately large production of LACTIC ACID, which latter then favors the *Solution* of the SANTONIN and its *Absorption* into the organism.

SANTONIN-OXIM, on the other hand, in virtue of its *Slight Solubility and Absorbability*, offers the greatest likelihood, among ALL Santonin Preparations, of accomplishing the removal of the Intestinal Parasites *without injury to the Patient!*

THE MYDRIATIC ALKALOIDS

of the Solanaceæ.

[BEGUN IN SEPTEMBER NUMBER; TO BE CONTINUED IN NOVEMBER.]

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THE MYDRIATIC ALKALOIDS

of the Solanaceæ.

ALSO:

THEIR NARCOTIC AND OTHER USES;

as Hypnotics, Sedatives, etc.

[CONTINUED FROM SEPTEMBER NUMBER.]

2.—Hyoscyamine.

HYOSCYAMINE ALKALOID may be obtained principally from the *leaves* and *seeds* of *Hyoscyamus niger*,—of late also from *Atropa belladonna* [see BULLETIN for September, page 70 !]. In the Drug-trade to-day THREE MODIFICATIONS of this preparation are met-with, to wit:

A.—**Amorphous Hyoscyamine,** not colorless;—*from Hyoscyamus niger;*—

B.—**Crystallized Hyoscyamine from Hyoscyamus niger,**—chemically pure, perfectly white, very light;—*consisting of* PURE HYOSCYAMINE ALKALOID *only;*—

C.—**"Commercial" Hyoscyamine,** *chemically identical with the preceding kind,* BUT OBTAINED **from Atropa belladonna.**

Besides these different modifications of HYOSCYAMINE ALKALOID, their **Sulphates, Hydrochlorates,** and **Hydrobromates** are also found in commerce; but **The Alkaloid** is what Modern Therapy has *principally* dealt with.

—AMORPHOUS HYOSCYAMINE is a light-brown, syrupy liquid, of alkaline reaction; *little soluble* in Water; *readily so* in Acidulated Water, in Alcohol, in Ether, and in Chloroform.

CRYSTALLIZED HYOSCYAMINE is in silky crystals, permanent in the air, melting at 108.5° C [227.3 F]; with *the same solubility-relations* as the foregoing kind.

"COMMERCIAL" HYOSCYAMINE, FROM ATROPA BELLADONNA, in its *physical* and *chemical* properties, is quite similar to the last-mentioned modification;—its PHYSIOLOGICAL and THERAPEUTICAL behaviors have not yet been reported-on.

— Some **Salts**, *both* of TRUE HYOSCYAMINE FROM HYOSCYAMUS NIGER *and* of "COMMERCIAL" HYOSCYAMINE FROM ATROPA BELLADONNA, can be produced in a well-crystallized form.

— —Generally speaking, the **Physiological and Therapeutical effects of Hyoscyamine** are *similar to those of* ATROPINE,— especially as regards *Mydriatic* action; still, in *recent* practice, its use for OPHTHALMOLOGY *has been nearly abandoned;* and it is now *principally* employed as a **Hypnotic** in *Mental disorders*, or as an **Anodyne** and **Antispasmodic** in *Asthma*, *Tussicular Irritation*, *Epilepsy*, *Colics*, *Chorea*, —being administered *either* SUBCUTANEOUSLY *or* BY MOUTH.

According to GNAUCK (*Paper read* at the Annual Meeting of the SOCIETY OF GERMAN PSYCHIATERS, at Eisenach, Sept., 1882) the **Pure Crystallized Hyoscyamine Alkaloid** *is the most eligible form* of this medicament,—as follows:

Dose, Subcutaneously:

0.005–0.01 gramme [1/12–1/6 grain];—*maximal:* 0.02–0.025 gramme [3/10–2/5 grain];—

Dose, Internally:

One and one-half times or twice as great as the SUBCUTANEOUS.

According to BARDET and EGASSE (*Formulaire des Nouveaux Remèdes*, 1888; p. 176), the DOSE for **Amorphous Hyoscyamine** is placed at 0.005–0.01 gramme [1/12–1/6 grain], and *may be gradually increased*, up to 0.05 gramme [3/4 grain].

— According to H. MIETH (*Inaugural Dissertation*, Leipsic, 1888; p. 28), the **Principal Indications** FOR THE USE OF HYOSCYAMINE are stated, with general agreement, as follows:

> "*Maniacal Excitation*, especially in Chronic and Periodic Manias.— Furthermore, apparently good results have been attained in *Epileptic* and *Menstrual* Excitations, in *Frenzy* Excitation, and in the *Motorial Unrest* of Dementia.—NO EFFECT has been accomplished by this medicament in the *Consternations of Melancholia;* its utility appears DOUBTFUL in *Paralysis*."

Counter-indications are: Heart and Vascular diseases; defective Nutrition; great physical Atony;—*psychically:* Vivid Hallucinations, especially of the Visual sense, with corresponding Phantasms.

—In POISONING BY HYOSCYAMINE, the *Autopsy reveals little* that is characteristic.—According to LEWIN, the prime passages exhibit Rubescence and conspicuous Venous Hyperemia.

The **Antidotal treatment** in such Poisoning proceeds on the principles laid-down for ATROPINE ANTIDOTING (see BULLETIN for September, page 72).

[TO BE CONTINUED.]

Antipyrine and Nitrites,—their Incompatibility!—According to KNORR,—when an ACIDULATED AQUEOUS SOLUTION of ANTIPYRINE is brought into contact with POTASSIUM NITRITE, a poorly soluble crystalline substance of *blue-green* color is formed; to wit,—*Iso-nitroso-Antipyrine:* $C_{11} H_{11} N_3 O_3$.

The researches of H. C. WOOD and J. MARSHAL have shown *this latter compound* to be DEVOID OF ANY ACTION, either on dogs or on rabbits. These investigators have given dogs 1–2 grammes [15–30 grains] of *Iso-nitroso-Antipyrine* by mouth, and have injected rabbits with 15 grammes [½ fl. oz.] of a saturated (0.375-%) Solution *of the same*, WITHOUT ANY DELETERIOUS EFFECTS being noticeable.—Furthermore,—a dog being given ANTIPYRINE, followed very soon by ETHYL NITRITE,—no abnormal condition whatever was manifested.

—**These negative results** cast *a new light* on the well-known fact of the INCOMPATIBILITY OF ANTIPYRINE WITH THE NITRITES (as, for instance, with Ethyl Nitrite); which light may prove of service to the Practitioner.

For, on the one hand, as above shown, ANTIPYRINE would seem to be capable of *diminishing, and even wholly neutralizing, the possible detrimental action of a* NITRITE; while, on the other hand, ANTIPYRINE *itself is debarred from all action* by the presence of sufficient NITRITE.—(*Centralblatt für die gesammte Therapie.*)

[The principal purpose of the above discussion seems to be, *to disabuse Physicians of the superstition*,—largely prevalent previous to Prof. WOOD'S and Dr. MARSHAL'S labors, as quoted,—*that the described blue-green compound*, formed by mixing ANTIPYRINE with a NITRITE, *is poisonous!*—ED.]

Bromoform — $CHBr_3$ — is, as its formula shows, *an Analogue to* CHLOROFORM ($CHCl_3$),—the three atoms of Bromine in the former taking the place of the three atoms of Chlorine in the latter. It appears as a colorless, limpid liquid, of a peculiar, sweetish, *agreeable taste.* It is *easily soluble* in Alcohol; *very poorly so* in Water,—5–6 drops dissolving in 100 grammes [3 1/4 fl. oz.] of water only after long and violent shaking. This AQUEOUS SOLUTION, if well corked, *may be preserved* for a long time.

BROMOFORM is an **Anesthetic**, like CHLOROFORM; while NOT *irritating the Mucous Membranes* of the mouth, as the latter does!

According to experiments made by HORROCH (*Oesterreichisches Medizinisches Jahrbuch*, 1883; p. 497) on a great variety of *animals* and on *Human patients*, COMPLETE ANESTHESIA was obtained by *much smaller* RESPIRATORY *doses* of BROMOFORM than of CHLOROFORM!

—**Also by Internal and by Subcutaneous Exhibition** of BROMOFORM, warm-blooded animals were placed in *Narcoses* lasting from 4 to 8 hours. Such Narcoses were induced within 5 to 36 minutes after the SUBCUTANEOUS administration of 0.1–1.0 gramme [1 1/2–15 grains] of BROMOFORM, and were always accompanied by a *Fall of Temperature* of from 3 to 5° C [5 1/2–9° F].

— —Recently, Dr. STEPP (*Deutsche Medizinische Wochenschrift*, 1889; No. 31) has *successfully treated* **Whooping-Cough** with BROMOFORM.—With **Internal** administration, Dr. STEPP remarked *no untoward symptoms whatever*, nor even any reaction on *Pulse* or *Temperature!*

Children's DAILY Dose:

5–10–20 DROPS; *dissolved* in about 100–120 grammes [3 1/4–4 fl. oz.] of *liquid;* preferably with the addition of a little Alcohol.—See following—

Formula:

BROMOFORM 10 drops; Alcohol 3–5 grammes [1–1 1/2 fl. dr.]; Distilled Water 100 grammes [3 1/4 fl. oz.]; Syrup 10 grammes [2 fl. dr.].—*One to Two Tablespoonfuls every hour!*

By such a form of SOLUTION, which the little ones readily take, Dr. STEPP *regularly obtained cures* of WHOOPING-COUGH within 4 weeks at most, in children of 6 months to 7 years. After as little as 5 or 6 days' treatment, *the attacks began to diminish* in frequency and intensity; and

in 10 days more, in most cases, *they ceased wholly.* Very severe cases, showing 30–40, or more, violent paroxysms per day, would require 10–12 days' BROMOFORM treatment before a diminution of the number set-in. *Then*, however, the reduction of the frequency was *very rapid*, accompanied by an *equally sudden* decrease of severity, and followed by an *early* complete cessation.

—A REMARKABLE PHENOMENON was noticed in this treatment; to wit: *the slight extent or entire absence of Pulmono-Catarrhal Symptoms;* and —when they existed—*their extremely rapid subsidence.*

Complications were NOT found by Dr. STEPP.

—Dr. GOLDSCHMIDT (*source as above quoted!*) also procured the complete cure, within a fortnight,—exclusively by the BROMOFORM treatment,—of some hopeless-appearing cases of children taken with exceptionally severe attacks of WHOOPING-COUGH *complicated with Pneumonia.*

Bryonia alba [*not* "DIOICA"!],—*recently found to be a* **Most Powerful Hemostatic**;—*and its Active Constituent:* **Bryonidin** [*not:* "BRYONIN"!].—Z. PETRESCU and ELIAU (*Deutsche Medizinische Zeitung*, 1889; p. 487) extol the merits of WHITE BRYONY (*Bryonia alba*) as a HEMOSTATIC *of Prime Efficacy!*—[This appears to be a *new use* for the drug.]

Their THERAPEUTIC DOSE of the DRY ROOT consisted of 20–25 grammes [5–6½ drams], *infused* in 300 grammes [10 fl. oz.] of hot Water, and *boiled down* to 150 grammes [5 fl. oz.]. Mixed with Syrup, this DECOCTION was given *in* 3–4 *half-hourly portions.*

—In the course of their investigations, P. and E. succeeded in isolating from the BRYONY ROOT, besides various Resins and Acids, also a *Glucosidal* body which they took to be BRYONIN, and whose general action corresponded to that of the Root.

They do NOT appear, however, to have isolated *the actual active constituent* of the Root; for A. MANKOWSKY (*Inaugural Dissertation;* Dorpat, 1889) reports having obtained TWO GLUCOSIDES from BRYONIA ALBA; to wit,—**Bryonin, and Bryonidin!** According to MANKOWSKY, **only the latter possesses Toxic** (*and hence Therapeutic!*) **properties.** He pronounces ALL *the substances* isolated by preceding investigators (VAUQUELIN, DULONG, FRÉMY, BRANDES and FIRNHABER, etc.), and by

them named "BRYONIN", to have been nothing but more or less purified *Extracts*, which possibly *contained* the real Glucosides!

—The **Aqueous** and the **Alcoholic Extract** of BRYONIA ALBA were also employed therapeutically by PETRESCU and ELIAU; and *especially the* ALCOHOLIC EXTRACT *was found* PRE-EMINENTLY EFFICACIOUS IN *Hematuria, Hemorrhages, Hemoptysis, Hematemesis, and Epistaxis;* being given in DOSE of 2–3 grammes [30–45 grains] PER DAY.

—**N. B.**—IT IS TO BE CAREFULLY NOTED (inasmuch as the *U.-S. Pharmacopœia* and other works *fail to make any practical distinction* between two leading varieties of BRYONY!), that **only the Bryonia alba** ("White Bryony") **is efficacious,** as above described; while *its closely related congener*, **the Bryonia dioica**—or, "*Red Bryony*"—(which may readily be confounded therewith) POSSESSES NO HEMOSTATIC VIRTUES!

—According to the *Animal experiments* made by PETRESCU and ELIAU, the **Physiologic action** of BRYONIA ALBA consists of a *Progressive Contraction of the Capillaries*, which may be continued until a Complete Arrest of the Circulation is secured! (This effect, on which its HEMOSTATIC application is based, appears to be procured through the intermedium of the *non-striated* muscle-fibers; whence it is most strongly manifested in organs containing a large proportion of that class of fibers.)

—For **Efficacy of Antihemorrhagic action,** PETRESCU and ELIAU place the WHITE BRYONY *ahead of all known Antihemorrhagics;* such as ERGOT, WITCH-HAZEL, etc.

Chloral-amide,—a recently discovered, *synthetically prepared* **Hypnotic,**—is composed by the *addition* of ANHYDROUS CHLORAL [$C Cl_3 . C H O$] to FORM-AMIDE [$C H O . N H_2$].

—Its formula is:

$$C Cl_3 . C H < \begin{matrix} O H \\ N H . C H O \end{matrix} \Big).$$

CHLORAL-AMIDE is in colorless crystals, *soluble* in 9 parts of Water; likewise in 1 1/2 parts of 96-% Alcohol. Its *taste* is mild, slightly bitter, not caustic.—Its AQUEOUS SOLUTION *must be prepared cold*, as the compound decomposes when heated above 60° C [140 F].—Its Aqueous and Alcoholic Solutions are not affected by either Weak Acids or Silver

Nitrate Solution; by Caustic Alkalis they are decomposed rapidly; and slowly by Alkali Carbonates.

— CHLORAL-AMIDE has so far been tested for **Therapeutic use** by HAGEN and HÜBNER; also by LETTOW, RABOW, REICHMANN, and by EUGEN KNY.—The results are condensed as follows (*Wiener Medizinische Presse*, 1889; p. 1361):

> "1.— CHLORAL-AMIDE was shown to be a *useful*, albeit *not universally efficacious*, **Hypnotic.**—In *Adults*, the effect was obtained within $^1/_2$ to 1 hour after a DOSE of 2–3 grammes [30–45 grains].
>
> "2.—The best results were obtained in *Nervous Agrypnia*, *Insomnias* caused by *Spinal affections*, in *Bronchial Asthma*, *Subacute Articular Rheumatism*; also in *Gastric affections not* coupled with *intensive pain*.
>
> "3.—**Accessory Effects,**—such as Headache, Vertigo, Lassitude,—were noticed *in several patients* on the following day.
>
> "4.—In those cases where a comparison could be made *between the actions of* CHLORAL HYDRATE *and of* CHLORAL-AMIDE, it resulted *to the advantage of* CHLORAL-AMIDE.
>
> "Professor RABOW, of Lausanne, (*Centralblatt für Nervenheilkunde*, 1889; No. 15) procured satisfactory effects *on himself* by DOSES as low as 1 gramme [15 grains]; for *Insane Patients*, however, the doses varied from 1 to 4 grammes [15 to 60 grains].— Sleep would be induced in 25–30 minutes after dosing, and would continue for 6–8 hours.—As a SEDATIVE *in highly excited patients* and in *Frenzied Maniacs*, doses of 3–4 grammes [45–60 grains] were found UTTERLY DEVOID OF EFFECT; the **Hypnotic action** *was most desirably manifested in Nervous Insomnia*, *Neurasthenia*, and similarly constituted disorders.— 3 grammes [45 grains] of CHLORAL-AMIDE were found to be equal, in active strength, to about 2 grammes [30 grains] of CHLORAL HYDRATE.—DISAGREEABLE ACCESSORIES *were not noticed* by RABOW after the use of CHLORAL-AMIDE."

— CHLORAL-AMIDE may be taken internally *in Powder*. (For this form, 1–3 grammes [15–45 grains] of the medicament are *triturated with* 1 gramme [15 grains] of FENNEL-OIL SUGAR [*Elæosaccharum Fœniculi*,— see "NATIONAL FORMULARY", No. 274]; OR, being triturated *alone*, are *inclosed in Wafers*.)—The dose is *followed* by a draught of Milk, Water, or Coffee.

Other Formulas:

1.—*Mixture for* INTERNAL *Dose.*

CHLORAL-AMIDE 3 grammes [45 grains]; *Diluted* Hydrochloric Acid

6 drops; Distilled Water 60 grammes [2 fl. oz.]; Raspberry Syrup 10 grammes [2 fl. dr.].—*To be taken all at one time!*

2.—*Mixture for* ENEMA!

CHLORAL-AMIDE 3 grammes [45 grains]; *Diluted* Hydrochloric Acid 2 1/2 drops; Alcohol 1 gramme [20 minims]; Distilled Water 100 grammes [3 1/4 fl. oz.].—*To be used as a Clyster!*

Mercury preparations;—their Relative Toxic Strengths compared.—ZEISING, of Breslau, at the First Congress of the GERMAN DERMATOLOGIC SOCIETY (Prague; June 10–12, 1889) reported on a carefully conducted series of *Animal-experiments*, made by him in order to determine the RELATIVE INTENSITIES OF TOXIC ACTION shown by various MERCURY COMPOUNDS. Rabbits were used as objects; and the following table shows the **Doses in Grammes-per-Kilogramme of the Animals' Weight** (or:—*grains of Dose per* 1000 *grains of Animal*) that were found requisite, of each substance named, *in order to make the animal die* under manifestations of the symptoms of MERCURY-POISONING.

LETHAL DOSE *per 1000 of Animal.*	MERCURY COMPOUND.
0.004–0.005	of the AMIDO-FORMATE.
0.005–0.01	" *Acidulated* Solution of CORROSIVE SUBLIMATE.
0.008–0.01	" *Aqueous* " " " "
0.01 –0.02	" the YELLOW OXIDE.
0.02 –0.04	" " SALICYLATE.
0.04	" " THYMOL-ACETATE.
0.06	" CALOMEL.

—From the above, it is evident that the **Absolute Mercury-strength** of each preparation *has less share in the result than the* **Degree of Resorbability** of the preparation into the organism!

——It is also noteworthy that the Administration by **Intraperitoneal Injection** was found to admit of *larger doses* than that of SIMPLY SUBCUTANEOUS INJECTION.

[With reference to INJECTIONS OF DIFFICULTLY SOLUBLE MERCURY COMPOUNDS, see the description of **Intragluteal Injections** on pages 6–7 of the present Volume; and Prof. NEISSER's remark about "**Intramuscular Injections**", on pages 81–82 of the same.—ED.]

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THE MYDRIATIC ALKALOIDS

of the Solanaceæ.

ALSO:

THEIR NARCOTIC AND OTHER USES;

as Hypnotics, Sedatives, etc.

[CONTINUED FROM NOVEMBER NUMBER.]

3.—Hyoscine.

This Alkaloid was discovered by LADENBURG in the mother-liquor remaining from the manufacture of HYOSCYAMINE.

HYOSCINE ALKALOID has never been obtained in crystalline, or even solid, form. It is a syrupy liquid, *difficultly soluble* in Water; *easily so* in Alcohol and in Ether.

It yields **well-crystallizable Salts**, among which the following are at present recognized as possessing **Therapeutic value**:

Hyoscine Hydrochlorate;
Hyoscine Hydrobromate;
Hyoscine Hydro-iodate.

The **Pure Hyoscine Alkaloid**, in consequence of its physical properties, *is not employed in Medicine*, and hence is not met-with in the Drug-trade.

All the Salts of Hyoscine are *soluble in Water;* and *insoluble* in *Strong* Alcohol and in Ether.

—In consequence of the *high therapeutic importance* of the HYOSCINE SALTS, and of the comparative lack of pharmacologic information regarding them in the books of the day, I shall treat them here at some length, and shall, for perspicuity, apportion the matter under several appropriate heads:—

A.—PHYSIOLOGIC EFFECTS.

Thorough researches on *warm-blooded* and *cold-blooded* animals were made by KOBERT and SOHRT, and also by KONRAD and SCHLEUSSNER. [The results of these are here condensed from a general review by A. CRAMER (*Münchener Medizinische Wochenschrift*, 1889; p. 365):]—

1.—**Ultimate Disposition made of Hyoscine by the Organism.**—"HYOSCINE is *eliminated* as such, or as a substance of same mode of action, *through the Kidneys.*"—[KOBERT.]

2.—**Effects on Pulse.**—Hereon the views of the investigators *differ!*—KOBERT and SOHRT found HYOSCINE HYDROCHLORATE *slightly accelerating* the Pulse, but *not otherwise notably affecting* it; *nor did* SCHLEUSSNER observe any material Pulse-effect.—KONRAD, on the other hand, experimenting with the same Salt, found *an initial Acceleration* (*not* in all cases, however!); but later-on (*and this in all cases!*) *a protracted Retardation* was noticed by him.—KLINKE *also* found HYOSCINE HYDRO-IODATE—*subcutaneously* administered to himself and to various Insane patients—to produce *Retardation* of Pulse.

3.—**Effects on Respiration.**—According to KOBERT and to SCHLEUSSNER, the Respiration *is not materially affected;* while KLINKE observed it *to be retarded.*

4.—**Spinal Cord.**—"It does *not* appear to be specially affected."—[KOBERT.]

5.—**Electrical Susceptibility of the Motorial Region of the Brain.**—"In the normal Dog, HYOSCINE gave *no* effect."—[KOBERT.]

6.—**Dilatation of the Pupil.**—*All the investigators agree in observing this*, to a greater or less extent, *in most cases.*

7.—**Salivary Secretion.**
8.—**Perspiration.** } —*All the investigators agree* in noticing their *Reduction.*

B.—OPHTHALMOLOGIC USE.

Soon after the discovery of HYOSCINE, experiments as to its *Therapeutic usefulness* were instituted,—both as regards OPHTHALMOLOGY and INTERNAL MEDICATION.

The first researches on its *Ophthalmologic use* were made by HIRSCHBERG in 1881. He drew from them the conclusion that HYOSCINE is a **Very Powerful Mydriatic**; but that, with regard to its ready liabil-

ity *to act on the organism generally*, caution ought to be exercised in its Ophthalmologic exhibition.

EMMERT (*Archiv für Augenheilkunde*, 1882; p. 183), and WALTER (*Inaugural Dissertation;* Dorpat, 1887), after manifold investigations, came to fully indorse HIRSCHBERG'S judgment; and EMMERT recommends the use of HYOSCINE in all cases where *energetic and prompt Mydriatic action* is desired.

C. WALTER found that *a more rapid and a greater Dilatation of the Pupil* was obtained from a $^1/_4$–1-% SOLUTION OF HYOSCINE than from a 1-% Solution of ATROPINE,—*the duration of the Mydriasis, however, being briefer.*

The same investigator also ascertained that the instillation of HYOSCINE *is quite eligible in Chronic Glaucoma;* while *Acute Glaucoma* is to be considered a COUNTER-INDICATION to the use of this Mydriatic.

—In OPHTHALMOLOGIC PRACTICE, *Solutions* varying **from 1:1000 to 1:400** are considered of eligible strength. Of the former strength, 10–15 *drops;* of the latter, 4–6 *drops*, are used for INSTILLATION at short intervals.

C.—GENERAL THERAPY.

HYOSCINE was first exhibited *internally* by EDLEFSEN and ILLING in 1881; then *internally and subcutaneously* by GNAUCK in the same year. Later-on, it was largely tested as to its *General Therapeutic virtues* by both British and American investigators. (Amongst the labors of the latter, the pioneer researches of Prof. Dr. H. C. WOOD, of Pennsylvania University, are worthy of special mention.)—I shall here quote, however, only from recent observations, as compiled by the above-mentioned report of A. CRAMER, which gives a lucid synopsis of all the latest experiences:—

> *In all the experiments* reported, the HYOSCINE employed was in the form of either **Hydrochlorate,** or **Hydrobromate,** or **Hydro-iodate.**—*No essential difference* in the MODES OF ACTION of these three Salts was reported!

Subcutaneous Dose.

"From 0.0001 to 0.002 gramme."—[KÜHLWETTER.]—(= $^1/_{650}$ to $^1/_{32}$ grain.)

—"Doses from 0.0005 to AT MOST 0.001 gramme" (=$^1/_{130}$ to *at most* $^1/_{65}$ grain) "have *in the majority* of cases proved *devoid of danger;* — HOWEVER, *there is a great difference of susceptibility* to the various doses between different individuals!"—[ERB; KNY; KLINKE.]

Hypodermic Accessories.

"*The Injections* were by some patients described as being *very painful.*" [KÜHLWETTER.]

Indications for Internal Medication.

According to ERB, *Internal administration* of HYOSCINE *acts less promptly* than Subcutaneous in NERVOUS DISEASES; but, according to DORNBLÜTH, KNY, KLINKE, *this drawback is compensated* by the *Internal* medication being *less dangerous*, and, especially in PSYCHOSES, *very enduring in its action!*

Internal Dose.

"May be made *larger than the Subcutaneous:* — up to 0.002 gramme" ($^1/_{32}$ grain).—"The *Strength of the Solution* is best proportioned so as to have 1 milligramme" ($^1/_{65}$ grain) "of HYOSCINE to a Tablespoonful of Menstruum."—[KNY.]

Administration without Patient's Knowledge.

"The above-indicated Strength of Solution is such that the Dose is *absolutely insipid;* which affords the sometimes very important possibility of *administering the medicament* to VERY MISTRUSTFUL PATIENTS *without their knowledge*, BY MIXING IT WITH THEIR FOOD!"—[KNY.]

Tolerance.

"A *protracted course* of administration causes INCREASE OF TOLERANCE."—[KÜHLWETTER; KONRAD; KNY.]

D.—HYPNOTIC ACTION.

KOBERT, in 10 INSANE patients, with EXCITATIONS and INSOMNIA, produced a 4 or 5 hours', or still longer, *Sleep* within 10–12 minutes after Injection, in almost every instance. *There were no disagreeable accessories.*

ERB observed the *Somnific effects* in many of his patients. Amongst others, the medicament was successful with a *Neurasthenic* sufferer, on whom a great number of other Hypnotics had wrought no effect.

WALTER, in employing the medicament OPHTHALMOLOGICALLY, found *no Hypnotic* action.

KÜHLWETTER satisfied himself that, *at first dosing, or within a brief period* of successive administrations, the medicament *never fails.* Even in the MOST INTENSIVELY EXCITED patients, *Complete Sedation*, immediately followed by *Sleep* of 6 to 8 hours' duration, was secured within 10 minutes. The patients *awoke without any ill effects* whatever; *after which* they lingered for an hour or two more in a dreamy *Semi-sleep.*

PITCAIRN reports excellent results (up to 19 hours' *Sleep*) in three cases; comprising,—DELIRIUM TREMENS, SENILE INSOMNIA, and AGITATED MELANCHOLIA.

SCHLEUSSNER recapitulates the results of *very numerous experiments* in the INSANE CLINIQUE OF STRASSBURG UNIVERSITY as follows:

> "*Notwithstanding the Difference in the Susceptibility* of various individuals to the Hypnotic action of HYOSCINE,—one needing more, another less, of the medicament to make him sleep;—and, *further*, *notwithstanding the partial Dependence of the Hypnotic Accession* on incidental circumstances, such as the Intensity of the Excitement prevailing through the day;—still, it may be accepted as a general rule that *Doses of* 0.5–0.6 *milligramme* [$^1/_{130}$–$^1/_{110}$ grain] are best adapted for producing a **protracted Sleep, characterized like the natural,** and *without evil accessory effects.*"

SALGÓ *declines to consider* HYOSCINE *a* HYPNOTIC *proper;* he finds that "the immediate and constant effect of HYOSCINE Injection *is not Sleep, but a condition greatly resembling Sleep.*"—This "somnolent" condition he describes as follows:

> "In the condition of the full HYOSCINE effect, *which is attained* 20 *minutes after Injection*, the patient lies *breathing calmly, though with deep puffs*, distending the corners of the mouth as in profound sleep. The *Pulse is vigorous*,—being fuller than before the Injection, though not notably accelerated. The entire *Muscular system is flaccid. Sensibility is not suspended;* but the reaction to surface impressions is slow and laborious.
>
> "In this condition the patients remain for varying periods,—*from two to eight hours.*—When they are approached, *they look up* listlessly and drowsily, murmuring indistinctly; but turning over again at once, with the declaration that they are 'sleepy'.
>
> "*A real, full Sleep*, however, is hardly attained. The patients are always found **somnolent, but yet awake.**"

DORNBLÜTH *almost invariably observed a quiet Sleep*, within a brief interval after the Dose, *when given in the evening.*

KNY finds HYOSCINE *preferable to other Hypnotics* in the treatment of EXCITED patients,—*provided it be given* INTERNALLY !

KLINKE, *from a series of* 1350 *experiments*, made on 69 INSANE patients *representing the most widely different forms of Disease*, **recapitulates** as follows :

> "HYOSCINE HYDRO-IODATE (as well as the HYDROCHLORATE and HYDROBROMATE), owing to its *Cheapness*, *Insipidity*, and *Convenience of Administration*, is often **preferable** — especially in DEMENTED or EXCITED patients — **to the other, more expensive and ill-tasting, Hypnotics** which are frequently used, and which are disliked even by ordinary patients."— [*Internally !* — ED.]

E.—SEDATIVE USES.

a.—IN EXCITATIONS OF INSANITY.

In 10 EXCITED MANIACS treated with HYOSCINE by KOBERT and SOHRT conjointly, *Sleep*, or at least, *Quiescence*, was *promptly procured* by the administration.

KÜHLWETTER — who would use this medicament *only* in a physically sound and vigorous individual — obtained *good effect* from it in the discrete and sudden paroxysms of CHRONIC MANIA and in the Excitations of MELANCHOLIA ; while, in ACUTE MANIA, on the whole, it proved *less efficacious.*

SCHLEUSSNER, in attempting to calm EXCITED patients *in the daytime*, had *less success;* — he thus obtained an actual Sedation in only 2 instances out of 18.

According to SALGÓ, *this medicament is sovereign* wherever the *prompt Sedation* of a FRENZIED MANIAC is desired,— especially, also, on account of the *Convenience* of its administration.

KONRAD holds HYOSCINE to be *at times eligible* in VIOLENT EXCITATIONS of CHRONIC MANIAS, especially in cases where the sufferer exhibits great Agility and Destructiveness. He then uses it in *Doses of* $^1/_2$–1 *milligramme* [$^1/_{130}$–$^1/_{65}$ grain].— On the other hand, he says, this medicament *should be avoided* in SANABLE ACUTE PSYCHOSES, *as long* as other Sedatives suffice.

Dornblüth used Hyoscine *with success* in Excitations of Mania.

Kny — especially with Internal administration (3000 *single doses in* 88 *patients*) — procured *Sedation and Sleep* in the most various conditions of Insane Excitation; *also in* Recent Manias he had the same success, and gained the impression that the *duration* of the malady was *abridged.*

Klinke saw *good results* especially in the Maniacal conditions of Paralysis; whereas in conditions of Melancholia he obtained *but little or no effect.*

b —IN NERVOUS DISORDERS.

Erb recognized Hyoscine as a **Most Excellent Palliative** in the Tremors of Paralysis agitans,— even in *very grave* cases. It afforded the sorely afflicted patients *eminent relief;* in one case even an actual *Remission* of the disease became apparent. In some patients Suspension of the Tremors of *several hours'* duration was secured. Also, Other Accessories of the Disease, such as Salivation, Hyperdiaphoresis, which were present in some of the cases treated, *remitted* for several hours.—The *Active Dose*, Subcutaneously, was of 0.2–0.3 milligramme [$^1/_{325}$–$^1/_{220}$ grain].

Kny procured *relief* for a patient of the above-described class by Internal medication with Hyoscine.

— Spasms of Individual Muscles and Muscular Groups (Cramps in the Facialis, the Accessorius; in the Muscles of the Back, Shoulder, and Abdomen) — although often of a very intensive and persistent character — *were relieved*, according to Erb,— in some cases transiently; in others for some hours. In one severe case of Torticollis convulsivus, treated by Erb, a surprising *Remission* took place. Also, in a very severe Hemiplegic Chorea, the same investigator obtained a considerable, though transient, *Sedation* of the morbid twitchings. In the latter case, however, Larger Doses had to be employed.

Kny procured *essential Abatement* of the torturing Muscular Spasms in the paralyzed leg of a sufferer from Compressile Myelitis, by *Doses of* 0.8 *milligramme* [$^1/_{80}$ grain].—In one case of Nervous Asthma he had but *indifferent success;* while in two cases of Alcoholic Tremor and Sudation he produced *rapid improvement* by *continued* Hyoscine medica-

tion.—The TREMORS OF MULTIPLEX SCLEROSIS were also *favorably affected* in several instances,—one of these developing into *permanent improvement.*—Also a case of WRITER'S CRAMP was noticed to be *greatly improved.*

F.—RECAPITULATION.

——According to the main consensus of the above-quoted reports, therefore, HYOSCINE *has established its character* as

A Useful Hypnotic and Sedative in Insane Excitations,

and as

A Desirable Palliative in certain Nervous Disorders;

—NEVERTHELESS, *its applicability is sometimes considerably restricted* by various ACCESSORY EFFECTS, observable at certain times or in certain individuals.

G.—ACCESSORY EFFECTS.

The property of this medicament, *of acting differently on different individuals,*—and also *differently on the same individual at different times,*—may be the cause of the various investigators' attaching such very different degrees of importance to this matter of the ACCESSORIES,—as they do.

—The experiments made by SOHRT on HEALTHY SUBJECTS—as communicated by KOBERT—showed *No Special Accessories* after Subcutaneous Doses of 0.5–1.0 milligramme [$^1/_{130}$–$^1/_{65}$ grain], *excepting Dryness in the Mouth and Dilatation of the Pupils.*—In INSANE PATIENTS, likewise, the experiments of these two investigators evolved *No Alarming Accessories* whatever.

ERB'S patients complained most of the following annoying sensations:—*Feeling of General Debility; Drowsiness; Flushed Face; Dry Throat; Slight Vertigo; Confusion; Indistinct Vision; Difficult Speech.* In one nervous lady an Injection of 0.6 milligramme [$^1/_{110}$ grain] induced a condition resembling *Drunkenness.*—ERB likewise observed that CONSUMPTIVES, to whom the medicament was given as an ANTI-SUDORIFIC, usually *bore it ill!*

KONRAD considered it of importance to state that HYOSCINE is capable of producing notable Disturbances of the *Heart-Innervation*, even by the usual therapeutic Doses. He also observed, *in addition to the Accessories* noted by ERB, occasional *Twitchings* in the arms (after

Doses of 0.5–1.0 milligramme [$^1/_{130}$–$^1/_{65}$ grain]); and the supervention of *Hallucinations,*—a phenomenon not devoid of danger to the Psychic condition.

KÜHLWETTER *likewise* notices this latter phenomenon, in addition to those previously described. Moreover, in *one* of his cases, a pretty considerable *Collapse* resulted after a comparatively small Dose. The patient in this case—a woman,—very shortly after the Injection, was *suddenly prostrated* as if lightning-struck.

In another case he witnessed very markedly pronounced *Gyrative movements* about the longitudinal axis of the body.

The occasional complaints of SCHLEUSSNER'S patients *were confined to* the previously quoted *General Symptoms* (Dry Throat, and Thirst; caused by Diminished Ptysmic Secretion); *except in three cases,* of which no nosologic particulars are given, and which, even by Medium Doses, (but still more by Doses of 1 milligramme [$^1/_{65}$ grain]) were affected as follows: *Giddiness; Buzzing; Headache; Pectoral Constraint; Dilated and Languid Pupils.*—Effects on the DIGESTIVE ORGANS were *not* noticed by SCHLEUSSNER.

An instance of *lightning-like rapidity* of the HYOSCINE action, as reported by KÜHLWETTER [above!], was also remarked by SALGÓ; who, however, observed *No Untoward Accessories* besides, and who found *but one instance* where the medicament was refused on account of *disagreeable sensations* following its use.

DORNBLÜTH observed *No Disagreeable Accessories besides* those reported by ERB.

KNY, after finding himself hampered in 6 patients by the *Accessory effects of* **Subcutaneous Injection,**—*such as:* Vacillating carriage; great Faintness; Gibbering speech; Illusions, etc.,—was thereby led to try **Internal Dosing**; WHEREBY ALL THESE PHENOMENA *were reduced to Utter Insignificance!*

H.—GENERAL SUMMARY.

KLINKE gives the following:

> "HYOSCINE, then, *relaxes* the MOTORIAL and SECRETORIAL Centres: *retards* the PULSE and RESPIRATION; produces *Dryness* of the MOUTH, *Dilatation* of the PUPILS;—*occasionally: Loss* of APPETITE; VOMITION.—This medica-

ment doubtlessly induces ILLUSIONS,—partly of a *Consternative* nature (INTROSPECTION !),—partly of a *Cheerful* character; EXISTING Illusions are *intensified* and *multiplied* by it.

"It will, therefore, be correct policy to *circumscribe* the use of HYOSCINE in RECENT PSYCHOSES; while it may be *very readily chosen*—even as to *increased Doses*—in ASTHENIZED PATIENTS,—*provided* NO HEART-COMPLICATION WHATEVER be present!"

I.—CONFIRMATION BY OTHER AUTHORITIES.

——*The foregoing coincides with* the views of the PHYSICIANS-IN-CHIEF of several large INSANE ASYLUMS, from whom I have recently procured personal expressions of judgment on the use of HYOSCINE.

Thus, Dr. DORNBLÜTH, and the MEDICAL CHIEFS of the INSANE ASYLUMS at Buda-Pesth, Leubus, Alt-Scherbitz, Stefansfeld, Nietleben, etc., etc.,—all of whom employ HYOSCINE in their institutions on a large scale,—expressed their concurrence, in general, with what is above stated. [I may recur in detail to the views of these gentlemen in a future number.]

J.—LITERATURE QUOTED-FROM.

1.—R. KOBERT: *Archiv für Experimentelle Pathologie und Pharmacie;* Vol. XXII, p. 396.
2.—W. ERB: "Ueber Hyoscin,"—*Therapeutische Monatshefte;* Vol. I, p. 252.
3.—KOBERT: (*the same*), p. 267.
4.—C. WALTER: *Inaugural Dissertation;* Dorpat, 1887.
5.—E. KÜHLWETTER: *Irrenfreund;* Vol. XXIX, p. 97.
6.—PITCAIRN: *The British Medical Journal;* 1888, p. 75.
7.—A. SCHLEUSSNER: *Inaugural Dissertation;* Strassburg, 1888.
8.—J. SALGÓ: *Wiener Medizinische Wochenschrift;* Vol. XXXVIII, p. 746.
9.—E. KONRAD: Erlenmeyer,—*Centralblatt für Nervenheilkunde;* Vol. XI, p. 529.
10.—DORNBLÜTH: (*the same*), p. 992.
11.—E. KNY: *Berliner Klinische Wochenschrift;* Vol. XXV, p. 1001.
12.—O. KLINKE: Erlenmeyer,—*Centralblatt für Nervenheilkunde;* Vol. XII, p. 196.

[TO BE CONCLUDED BY "HOMATROPINE" IN NEXT NUMBER!]

Amyl Nitrite, Tertiary [!], (Bertoni's Amylo-nitrous Ether).—[*Additional to* BULLETIN for October, 1889:]

—*The* BOILING-POINT *of this liquid is* NOT, as stated on page 82 of the present Volume, "*about* 30° *C* [86 *F*]";—BUT, as Prof. BERTONI now states:

—33° C [199.4 F]!—

CLASSIFIED and DESCRIPTIVE
REGISTER OF CONTENTS.

Second Year (1889) of "Merck's Bulletin".

I.—Acids,—

"Organic" *and* "Anorganic".

II.—Alkaloids,—and other

Natural "Organic" Principles; *and* their *Compounds*, and *Derivatives.*

III.—Artificial Carbon-compounds—

by Synthesis *or* by Fractionation.

IV.—Drugs, and

their *Extracts* and *Compounds.*

V.—Metallic Salts,—and other "*Anorganic*" Compounds,—*except* those called "Acids".

VI.—Therapeutic hints, etc.

N.B.—*Only* the more *elaborate* or *important* matters of this class are listed here.

ALPHABETIC LIST OF CONTENTS.

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